123007

U.S. DEPARTMENT OF COMMERCE
Patent and Trademark Office

SEARCH REQUEST FORM

Requestor's Name: Hong Liu

Serial Number: 09/972,582

Date: 5/26/04

Phone: 2-0669

Art Unit: 1624

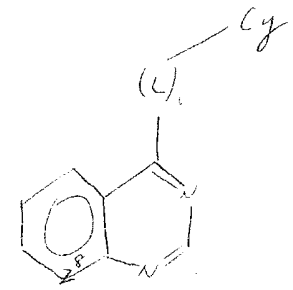
REMSCH 5C18

Search Topic:

Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevent citations, authors, keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevent claim(s).

Barb please

1 method of inhibiting p38a activity



2: N or C

Quinazoline Derivs

S. Chakravarty

S. Dugar

J. Perumattam

STAFF USE ONLY

Date completed: 6-4-04

Searcher: BOB

Terminal time: 23

Elapsed time: prep 20

CPU time:

Total time:

Number of Searches:

Number of Databases:

Search Site

- ____ STIC
- ____ CM-1
- ____ Pre-S

Type of Search

- ____ N.A. Sequence
- ____ A.A. Sequence
- 1 Structure
- ____ Bibliographic

Vendors

- ____ IG
- 582 STN
- ____ Dialog
- ____ APS
- ____ Geninfo
- ____ SDC
- ____ DARC/Questel
- ____ Other

=> fil reg; d stat que l8
FILE 'REGISTRY' ENTERED AT 12:38:52 ON 04 JUN 2004

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 3 JUN 2004 HIGHEST RN 689216-09-9
DICTIONARY FILE UPDATES: 3 JUN 2004 HIGHEST RN 689216-09-9

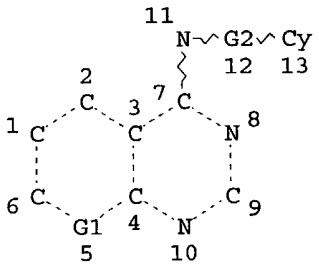
TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

L6 STR



VAR G1=N/C
REP G2=(0-1) C
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 13

STEREO ATTRIBUTES: NONE
L8 18991 SEA FILE=REGISTRY SSS FUL L6

100.0% PROCESSED 47557 ITERATIONS 18991 ANSWERS
SEARCH TIME: 00.00.02

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=> fil reg; d ide l5
FILE 'REGISTRY' ENTERED AT 12:38:59 ON 04 JUN 2004
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STRUCTURE FILE UPDATES:     3 JUN 2004  HIGHEST RN 689216-09-9
DICTIONARY FILE UPDATES:    3 JUN 2004  HIGHEST RN 689216-09-9

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html


L5   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   165245-96-5  REGISTRY
CN   Kinase (phosphorylating), protein, RK (9CI)   (CA INDEX NAME)
OTHER NAMES:
CN   CSBP
CN   CSBP kinase
CN   CSBP/p38 kinase
CN   Cytokine synthesis anti-inflammatory drug-binding protein
CN   High-osmolarity glycerol response kinase
CN   MAP kinase Hog1p
CN   Mitogen-activated protein kinase Mxi2
CN   P38 kinase
CN   p38 MAP kinase
CN   p38 MAPK
CN   p38 Mitogen-activated kinase
CN   p38 Mitogen-activated protein kinase
CN   P38-2 mitogen-activated protein kinase
CN   p38.alpha. MAP kinase
CN   p38.alpha. Mitogen-activated protein kinase
CN   p38/RK
CN   Protein kinase HOG1
CN   Protein kinase p38/HOG
CN   Protein kinase p38/HOG1
CN   Protein kinase p38mapk
CN   Protein kinase p38SAPK2
CN   Protein kinase RK
CN   Protein kinase SAPK2a
CN   Protein p38.alpha. kinase
CN   Reactivating kinase
CN   SAPK2a/p38 kinase
CN   Stress-activated protein kinase p38.alpha.
CN   Stress-activated protein kinase-2a
CN   Stress-activated-protein kinase-2
DR   185402-48-6, 185464-66-8
MF   Unspecified
```

CI MAN
SR CA
LC STN Files: ADISNEWS, AGRICOLA, BIOBUSINESS, BIOSIS, CA, CAPLUS, CASREACT, CEN, CIN, PROMT, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Conference; Dissertation; Journal; Patent; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); PROC (Process); PRP (Properties)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
5497 REFERENCES IN FILE CA (1907 TO DATE)
71 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
5523 REFERENCES IN FILE CAPLUS (1907 TO DATE)

```
=> fil capl; d que nos l13; fil uspatf; d que nos l21; fil medl; d que nos l35; fil
embase; d que nos l40
FILE 'CAPLUS' ENTERED AT 12:49:39 ON 04 JUN 2004
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FILE COVERS 1907 - 4 Jun 2004  VOL 140 ISS 24
FILE LAST UPDATED: 3 Jun 2004  (20040603/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE


L5             1 SEA FILE=REGISTRY ABB=ON  165245-96-5
L6               STR
L8         18991 SEA FILE=REGISTRY SSS FUL L6
L9          5522 SEA FILE=CAPLUS ABB=ON  L5
L10         5347 SEA FILE=CAPLUS ABB=ON  P38/OBI(3A)KINASE/OBI
L11          116 SEA FILE=CAPLUS ABB=ON  P38.ALPHA./OBI
L12         1321 SEA FILE=CAPLUS ABB=ON  L8
L13           17 SEA FILE=CAPLUS ABB=ON  L12 AND (L9 OR L10 OR L11)



FILE 'USPATFULL' ENTERED AT 12:49:39 ON 04 JUN 2004
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 3 Jun 2004 (20040603/PD)
FILE LAST UPDATED: 3 Jun 2004 (20040603/ED)
HIGHEST GRANTED PATENT NUMBER: US6745393
HIGHEST APPLICATION PUBLICATION NUMBER: US2004107471
CA INDEXING IS CURRENT THROUGH 3 Jun 2004 (20040603/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 3 Jun 2004 (20040603/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Apr 2004
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Apr 2004

>>>  USPAT2 is now available.  USPATFULL contains full text of the     <<<
>>>  original, i.e., the earliest published granted patents or         <<<
>>>  applications.  USPAT2 contains full text of the latest US         <<<
>>>  publications, starting in 2001, for the inventions covered in     <<<
>>>  USPATFULL.  A USPATFULL record contains not only the original     <<<
>>>  published document but also a list of any subsequent              <<<
>>>  publications.  The publication number, patent kind code, and      <<<
>>>  publication date for all the US publications for an invention     <<<
>>>  are displayed in the PI (Patent Information) field of USPATFULL   <<<
>>>  records and may be searched in standard search fields, e.g., /PN, <<<
>>>  /PK, etc.                                                         <<<
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>>>  USPATFULL and USPAT2 can be accessed and searched together        <<<
>>>  through the new cluster USPATALL.  Type FILE USPATALL to         <<<
>>>  enter this cluster.                                               <<<
>>>                                                                    <<<
>>>  Use USPATALL when searching terms such as patent assignees,       <<<
>>>  classifications, or claims, that may potentially change from     <<<
>>>  the earliest to the latest publication.                           <<<

This file contains CAS Registry Numbers for easy and accurate
substance identification.


L5             1 SEA FILE=REGISTRY ABB=ON  165245-96-5
L6               STR
L8         18991 SEA FILE=REGISTRY SSS FUL L6
L14         6910 SEA FILE=REGISTRY ABB=ON  L8 AND USPATFULL/LC
L15          430 SEA FILE=USPATFULL ABB=ON  L14
L16          298 SEA FILE=USPATFULL ABB=ON  L5
L17          323 SEA FILE=USPATFULL ABB=ON  (P38(3A)KINASE)/IT,TI,AB,CLM
L18           39 SEA FILE=USPATFULL ABB=ON  (P38.ALPHA.)/IT,TI,AB,CLM
L19           15 SEA FILE=USPATFULL ABB=ON  (P 38(3A)KINASE)/IT,TI,AB,CLM
L20            1 SEA FILE=USPATFULL ABB=ON  (P 38.ALPHA.)/IT,TI,AB,CLM
L21            8 SEA FILE=USPATFULL ABB=ON  L15 AND (L16 OR L17 OR L18 OR L19
                 OR L20)


FILE 'MEDLINE' ENTERED AT 12:49:39 ON 04 JUN 2004

 FILE LAST UPDATED: 3 JUN 2004 (20040603/UP).  FILE COVERS 1951 TO DATE.

 On February 29, 2004, the 2004 MeSH terms were loaded.  See HELP RLOAD
 for details. OLDMEDLINE now back to 1951.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2004 vocabulary.  See http://www.nlm.nih.gov/mesh/ and
 http://www.nlm.nih.gov/pubs/techbull/nd03/nd03_mesh.html for a
 description of changes.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


L6               STR
L8         18991 SEA FILE=REGISTRY SSS FUL L6
L23           10 SEA FILE=REGISTRY ABB=ON  MEDLINE/LC AND L8
L27          532 SEA FILE=MEDLINE ABB=ON  L23
L28           12 SEA FILE=MEDLINE ABB=ON  (P 38(3A)KINASE)
L29            1 SEA FILE=MEDLINE ABB=ON  (P 38.ALPHA.)
L30         5490 SEA FILE=MEDLINE ABB=ON  (P38(3A)KINASE)
L31           48 SEA FILE=MEDLINE ABB=ON  (P38.ALPHA.)
L32        14733 SEA FILE=MEDLINE ABB=ON  MITOGEN-ACTIVATED PROTEIN KINASES/CT
L34         2295 SEA FILE=MEDLINE ABB=ON  L32(L)AI/CT  AI = antagonists & inhibitors
L35            4 SEA FILE=MEDLINE ABB=ON  L34 AND L27 AND (L28 OR L29 OR L30 OR
                 L31)


FILE 'EMBASE' ENTERED AT 12:49:39 ON 04 JUN 2004
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FILE COVERS 1974 TO 4 Jun 2004 (20040604/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

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L6              STR
L8         18991 SEA FILE=REGISTRY SSS FUL L6
L24           15 SEA FILE=REGISTRY ABB=ON  EMBASE/LC AND L8
L28           12 SEA FILE=MEDLINE ABB=ON  (P 38(3A)KINASE)
L29            1 SEA FILE=MEDLINE ABB=ON  (P 38.ALPHA.)
L30         5490 SEA FILE=MEDLINE ABB=ON  (P38(3A)KINASE)
L31           48 SEA FILE=MEDLINE ABB=ON  (P38.ALPHA.)
L36         1382 SEA FILE=EMBASE ABB=ON  L24
L37         4181 SEA FILE=EMBASE ABB=ON  (L28 OR L29 OR L30 OR L31)
L39         3625 SEA FILE=EMBASE ABB=ON  PROTEIN TYROSINE KINASE INHIBITOR/CT
L40           10 SEA FILE=EMBASE ABB=ON  L36 AND L37 AND L39
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=> dup rem l13,l21,l35,l40
FILE 'CAPLUS' ENTERED AT 12:49:46 ON 04 JUN 2004
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FILE 'MEDLINE' ENTERED AT 12:49:46 ON 04 JUN 2004

FILE 'EMBASE' ENTERED AT 12:49:46 ON 04 JUN 2004
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PROCESSING COMPLETED FOR L13
PROCESSING COMPLETED FOR L21
PROCESSING COMPLETED FOR L35
PROCESSING COMPLETED FOR L40
L41           37 DUP REM L13 L21 L35 L40 (2 DUPLICATES REMOVED)
                 ANSWERS '1-17' FROM FILE CAPLUS
                 ANSWERS '18-24' FROM FILE USPATFULL
                 ANSWERS '25-28' FROM FILE MEDLINE
                 ANSWERS '29-37' FROM FILE EMBASE
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=> d ibib ed abs hitstr 1-24; d iall 25-37
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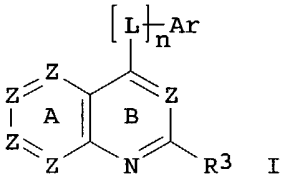
L41 ANSWER 1 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2002:845560 CAPLUS
DOCUMENT NUMBER: 137:353051
TITLE: Preparation of quinazolines as TGF-.beta. and/or **p38-.alpha. kinase** inhibitors
INVENTOR(S): Chakravarty, Sarvajit; Dugar, Sundeep; Perumattam, John J.; Schreiner, George F.; Liu, David Y.; Lewicki, John A.
PATENT ASSIGNEE(S): Scios, Inc., USA
SOURCE: U.S., 37 pp., Cont.-in-part of U.S. 6,184,226. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6476031	B1	20021105	US 1999-383825	19990827
US 6184226	B1	20010206	US 1998-141916	19980828
US 6277989	B1	20010821	US 2000-525034	20000314
US 2003069248	A1	20030410	US 2001-969936	20011002
US 2002161010	A1	20021031	US 2001-972582	20011005

PRIORITY APPLN. INFO.: US 1998-141916 A2 19980828
US 1999-383825 A3 19990827

OTHER SOURCE(S): MARPAT 137:353051
ED Entered STN: 07 Nov 2002
GI



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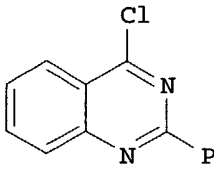

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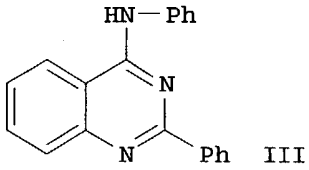

III

AB Title compds. I [R3 = (un)substituted arom.; Ar = (un)substituted monocyclic or polylcyclic arom.; L = S(CR22)m, NR1SO2(CR22)l, SO2(CR22)m, etc.; Z = CR2, N with the provisos that no more than two Z positions in ring A are N and wherein two adjacent Z positions in ring A cannot be N; R2 = H, alkyl, alkenyl, etc.; l = 0-3; m = 0-4; n = 1] and their pharmaceutically acceptable salts were prepd. For example, condensation of chloroquinazoline II and 4-aminopyridine afforded claimed quinazoline III. In p38-.alpha. kinase inhibition studies, 9-examples of compds. I exhibited IC50 values in the range of 0.1-1.5 .mu.M. Also, the specificity of compds. I for p38-.alpha. was assessed by their ability to inhibit other kinases, e.g., p38-y JNK1, PKA, PKC, PK(PKD), cck2 and EGF-R, with IC50 values ranging from 4.2 - >500 .mu.M. Compds. I are useful anti-inflammatory agents and in the treatment of fibroproliferative diseases.

IT **54665-94-0P 157862-99-2P 166039-38-9P**
259870-32-1P 259870-33-2P 259870-34-3P
259870-35-4P 259870-36-5P 259870-37-6P
259870-38-7P 259870-39-8P 259870-40-1P
259870-42-3P 259870-43-4P, 2-(2,6-Dibromophenyl)-4-(4-pyridylamino)quinazoline **259870-44-5P 259870-45-6P**, 2-(2-Fluorophenyl)-4-(4-pyridylamino)-6,7-dimethoxyquinazoline **259870-46-7P**, 2-(4-Fluorophenyl)-4-(4-pyridylamino)-6,7-dimethoxyquinazoline **259870-47-8P**, 2-(2-Fluorophenyl)-4-(4-pyridylamino)-6-nitroquinazoline **259870-48-9P**
259870-49-0P 259870-50-3P 259870-51-4P
259870-52-5P 308300-05-2P 404828-44-0P
420831-73-8P 422561-07-7P 438247-46-2P
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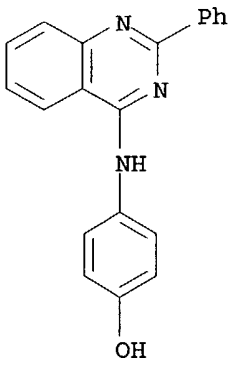
474289-95-7P 474289-98-0P 474290-00-1P
474290-02-3P 474290-04-5P 474290-06-7P
474290-07-8P 474290-08-9P 474290-09-0P
474290-15-8P 474290-17-0P 474290-19-2P
474290-23-8P 474290-26-1P 474290-28-3P
474290-30-7P 474290-32-9P 474290-38-5P,
2-(3-Methoxyphenyl)-4-(4-pyridylamino)quinazoline
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; prepn. of quinazolines as TGF-.beta. and/or **p38-.alpha. kinase** inhibitors)

RN 54665-94-0 CAPLUS
CN Phenol, 4-[(2-phenyl-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



RN 157862-99-2 CAPLUS
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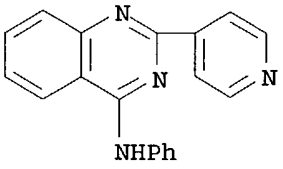

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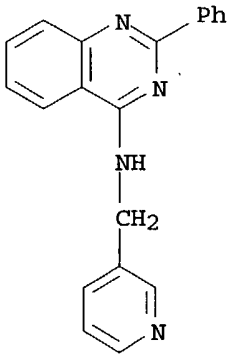

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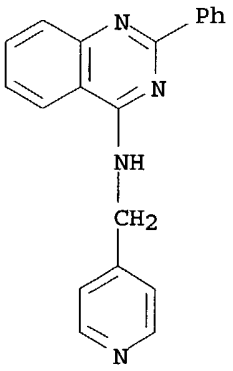

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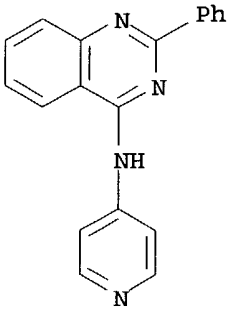

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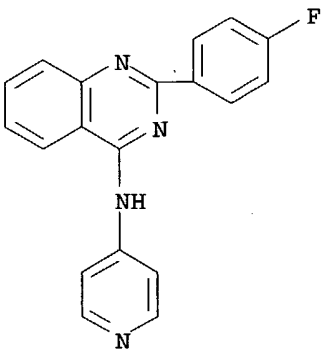

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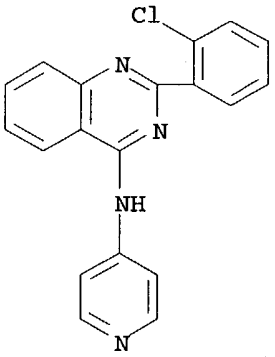

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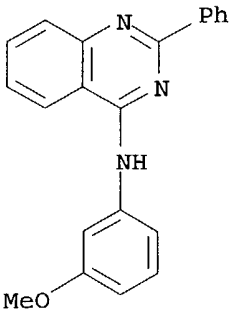
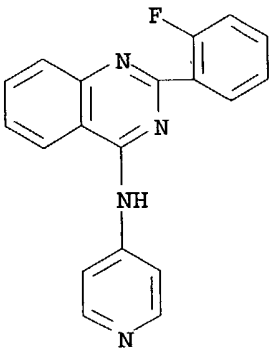
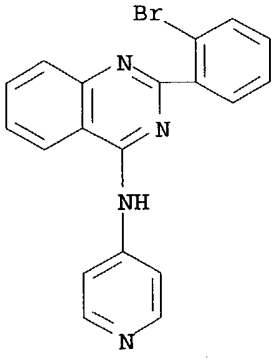


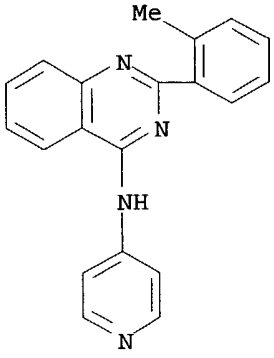
RN 259870-37-6 CAPLUS
CN 4-Quinazolinamine, 2-(2-fluorophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



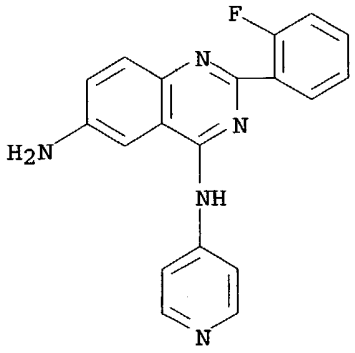
RN 259870-38-7 CAPLUS
CN 4-Quinazolinamine, 2-(2-bromophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



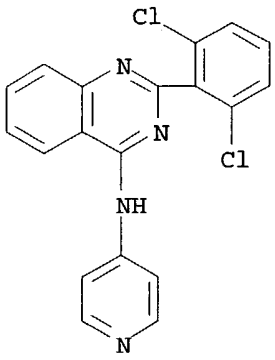
RN 259870-39-8 CAPLUS
CN 4-Quinazolinamine, 2-(2-methylphenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



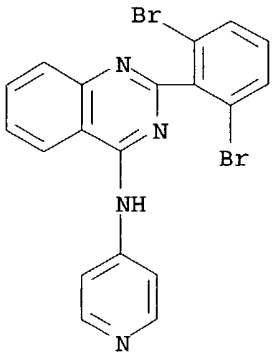
RN 259870-40-1 CAPLUS
CN 4,6-Quinazolinediamine, 2-(2-fluorophenyl)-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



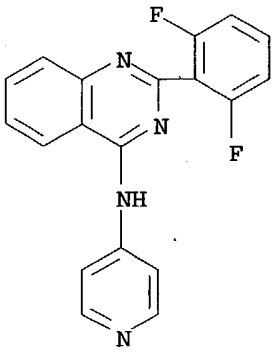
RN 259870-42-3 CAPLUS
CN 4-Quinazolinamine, 2-(2,6-dichlorophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



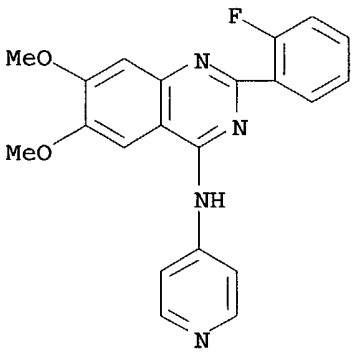
RN 259870-43-4 CAPLUS
CN 4-Quinazolinamine, 2-(2,6-dibromophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



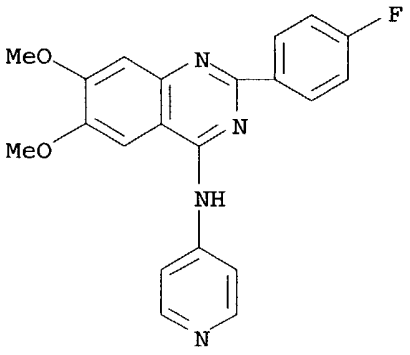
RN 259870-44-5 CAPLUS
CN 4-Quinazolinamine, 2-(2,6-difluorophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



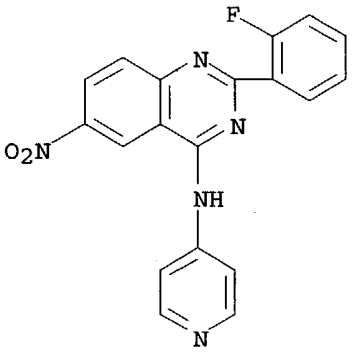
RN 259870-45-6 CAPLUS
CN 4-Quinazolinamine, 2-(2-fluorophenyl)-6,7-dimethoxy-N-4-pyridinyl- (9CI) (CA INDEX NAME)



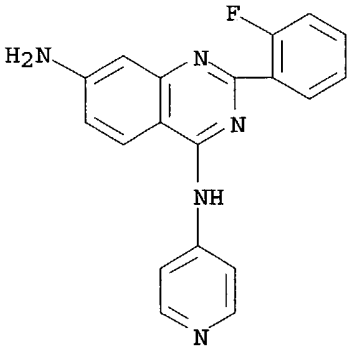
RN 259870-46-7 CAPLUS
CN 4-Quinazolinamine, 2-(4-fluorophenyl)-6,7-dimethoxy-N-4-pyridinyl- (9CI) (CA INDEX NAME)



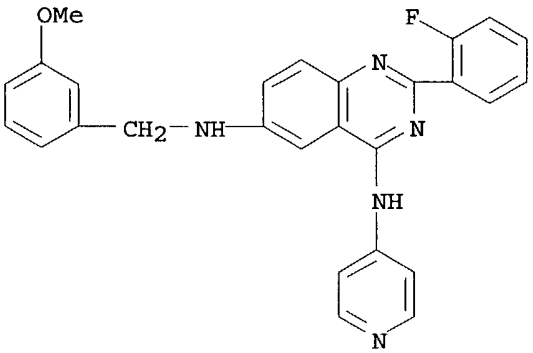
RN 259870-47-8 CAPLUS
CN 4-Quinazolinamine, 2-(2-fluorophenyl)-6-nitro-N-4-pyridinyl- (9CI) (CA INDEX NAME)



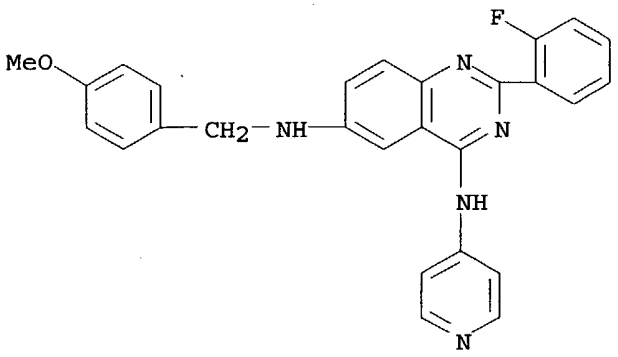
RN 259870-48-9 CAPLUS
CN 4,7-Quinazolinediamine, 2-(2-fluorophenyl)-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



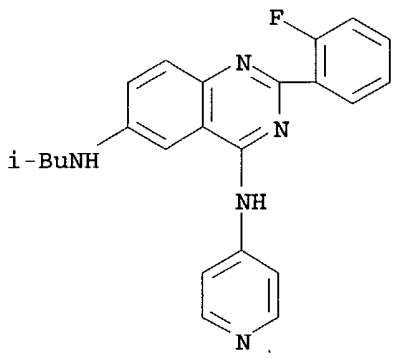
RN 259870-49-0 CAPLUS
CN 4,6-Quinazolinediamine, 2-(2-fluorophenyl)-N6-[(3-methoxyphenyl)methyl]-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



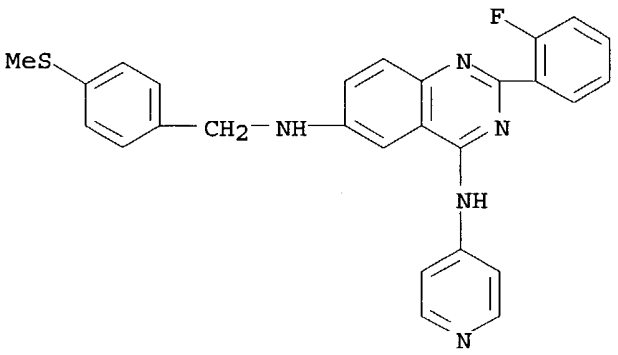
RN 259870-50-3 CAPLUS
CN 4,6-Quinazolinediamine, 2-(2-fluorophenyl)-N6-[(4-methoxyphenyl)methyl]-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



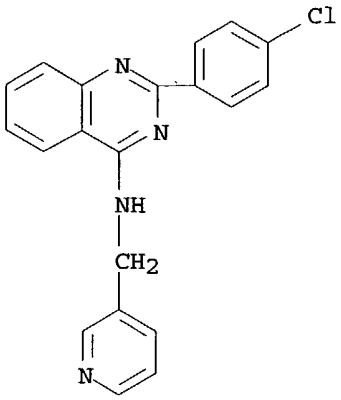
RN 259870-51-4 CAPLUS
CN 4,6-Quinazolinediamine, 2-(2-fluorophenyl)-N6-(2-methylpropyl)-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



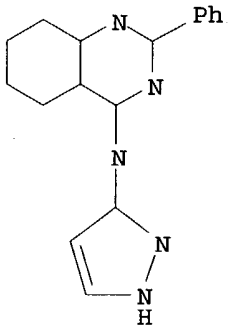
RN 259870-52-5 CAPLUS
CN 4,6-Quinazolinediamine, 2-(2-fluorophenyl)-N6-[[4-(methylthio)phenyl]methyl]-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



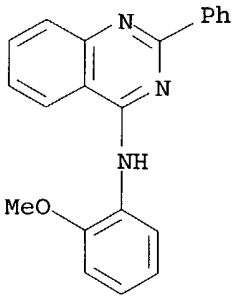
RN 308300-05-2 CAPLUS
CN 4-Quinazolinamine, 2-(4-chlorophenyl)-N-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



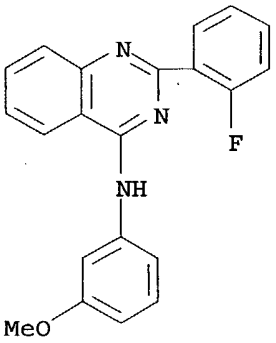
RN 404828-44-0 CAPLUS
CN 4-Quinazolinamine, 2-phenyl-N-1H-pyrazol-3-yl- (9CI) (CA INDEX NAME)



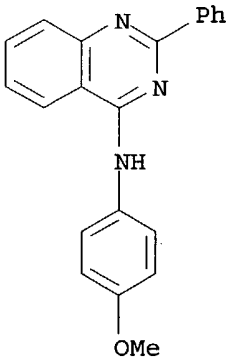
*** FRAGMENT DIAGRAM IS INCOMPLETE ***
RN 420831-73-8 CAPLUS
CN 4-Quinazolinamine, N-(2-methoxyphenyl)-2-phenyl- (9CI) (CA INDEX NAME)



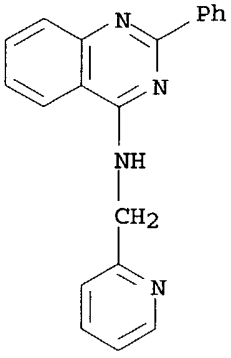
RN 422561-07-7 CAPLUS
CN 4-Quinazolinamine, 2-(2-fluorophenyl)-N-(3-methoxyphenyl)- (9CI) (CA INDEX NAME)



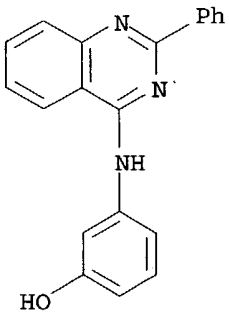
RN 438247-46-2 CAPLUS
CN 4-Quinazolinamine, N-(4-methoxyphenyl)-2-phenyl- (9CI) (CA INDEX NAME)



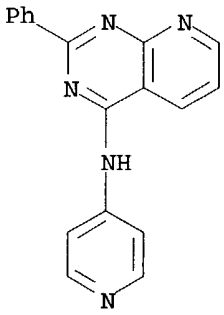
RN 446312-97-6 CAPLUS
CN 4-Quinazolinamine, 2-phenyl-N-(2-pyridinylmethyl)- (9CI) (CA INDEX NAME)



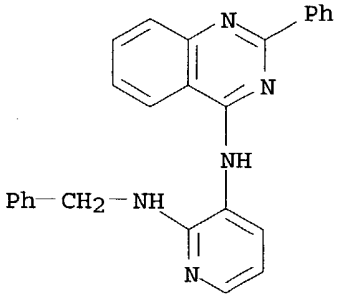
RN 446829-19-2 CAPLUS
CN Phenol, 3-[(2-phenyl-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



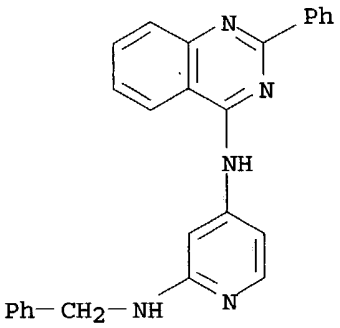
RN 474289-34-4 CAPLUS
CN Pyrido[2,3-d]pyrimidin-4-amine, 2-phenyl-N-4-pyridinyl- (9CI) (CA INDEX NAME)



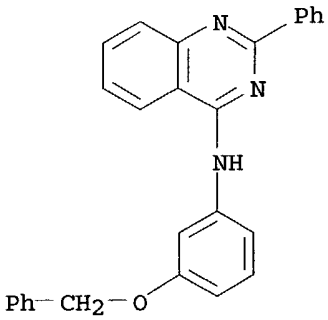
RN 474289-37-7 CAPLUS
CN 2,3-Pyridinediamine, N2-(phenylmethyl)-N3-(2-phenyl-4-quinazolinyl)- (9CI) (CA INDEX NAME)



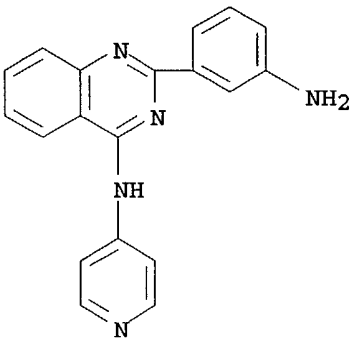
RN 474289-39-9 CAPLUS
CN 2,4-Pyridinediamine, N2-(phenylmethyl)-N4-(2-phenyl-4-quinazolinyl)- (9CI) (CA INDEX NAME)



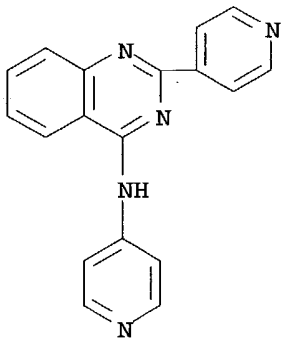
RN 474289-40-2 CAPLUS
CN 4-Quinazolinamine, 2-phenyl-N-[3-(phenylmethoxy)phenyl]- (9CI) (CA INDEX NAME)



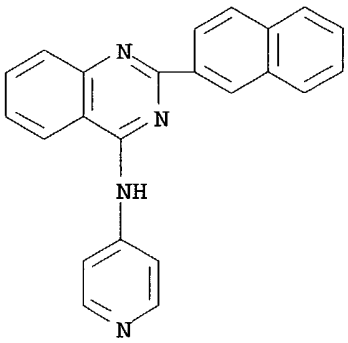
RN 474289-42-4 CAPLUS
CN 4-Quinazolinamine, 2-(3-aminophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



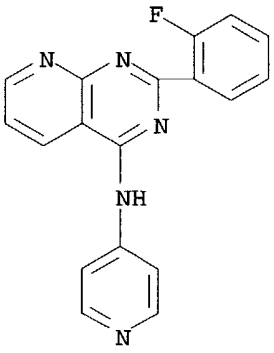
RN 474289-44-6 CAPLUS
CN 4-Quinazolinamine, N,2-di-4-pyridinyl- (9CI) (CA INDEX NAME)



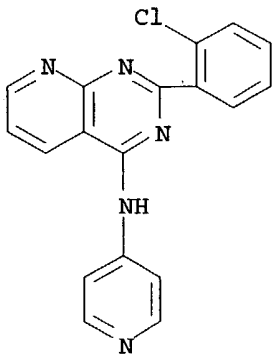
RN 474289-45-7 CAPLUS
CN 4-Quinazolinamine, 2-(2-naphthalenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



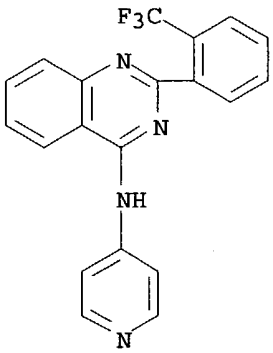
RN 474289-46-8 CAPLUS
CN Pyrido[2,3-d]pyrimidin-4-amine, 2-(2-fluorophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



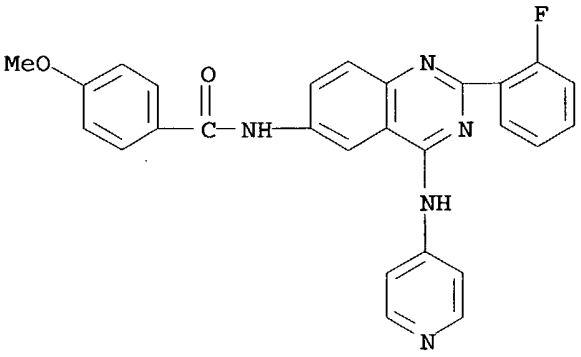
RN 474289-48-0 CAPLUS
CN Pyrido[2,3-d]pyrimidin-4-amine, 2-(2-chlorophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



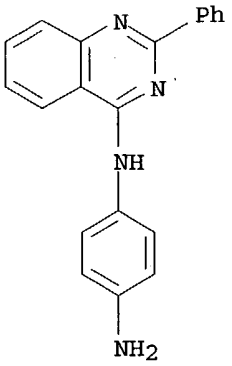
RN 474289-50-4 CAPLUS
CN 4-Quinazolinamine, N-4-pyridinyl-2-[2-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



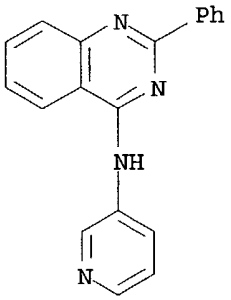
RN 474289-52-6 CAPLUS
CN Benzamide, N-[2-(2-fluorophenyl)-4-(4-pyridinylamino)-6-quinazolinyl]-4-methoxy- (9CI) (CA INDEX NAME)



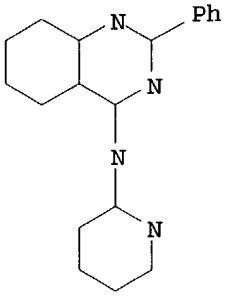
RN 474289-54-8 CAPLUS
CN 1,4-Benzenediamine, N-(2-phenyl-4-quinazolinyl)- (9CI) (CA INDEX NAME)



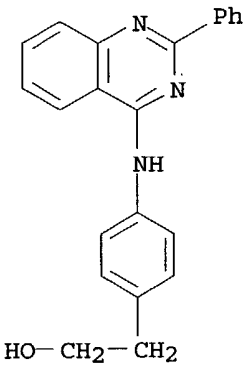
RN 474289-60-6 CAPLUS
CN 4-Quinazolinamine, 2-phenyl-N-3-pyridinyl- (9CI) (CA INDEX NAME)



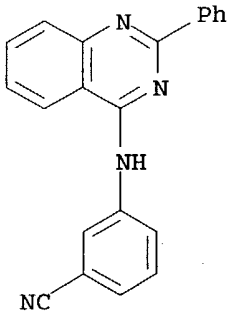
RN 474289-64-0 CAPLUS
CN 4-Quinazolinamine, 2-phenyl-N-2-pyridinyl- (9CI) (CA INDEX NAME)



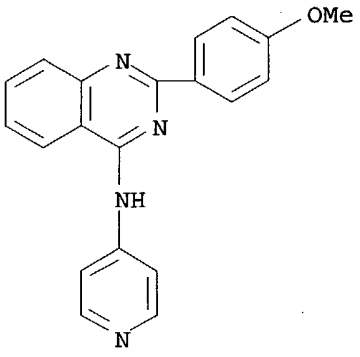
*** FRAGMENT DIAGRAM IS INCOMPLETE ***
RN 474289-68-4 CAPLUS
CN Benzeneethanol, 4-[(2-phenyl-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



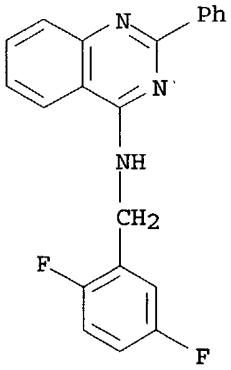
RN 474289-70-8 CAPLUS
CN Benzonitrile, 3-[(2-phenyl-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



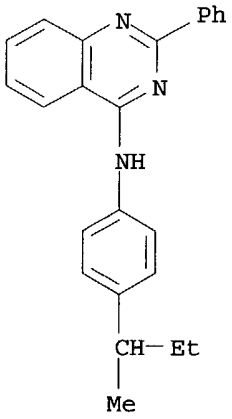
RN 474289-74-2 CAPLUS
CN 4-Quinazolinamine, 2-(4-methoxyphenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



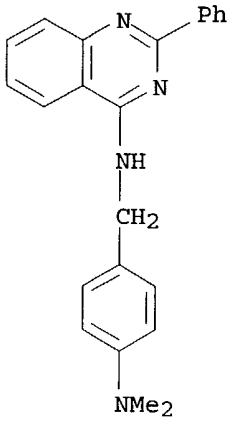
RN 474289-76-4 CAPLUS
CN 4-Quinazolinamine, N-[(2,5-difluorophenyl)methyl]-2-phenyl- (9CI) (CA INDEX NAME)



RN 474289-79-7 CAPLUS
CN 4-Quinazolinamine, N-[4-(1-methylpropyl)phenyl]-2-phenyl- (9CI) (CA INDEX NAME)

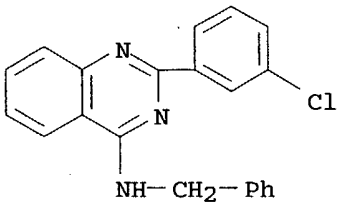


RN 474289-80-0 CAPLUS
CN 4-Quinazolinamine, N-[[4-(dimethylamino)phenyl]methyl]-2-phenyl- (9CI) (CA INDEX NAME)

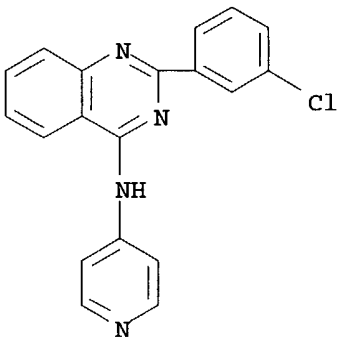


RN 474289-82-2 CAPLUS
CN 4-Quinazolinamine, 2-(3-chlorophenyl)-N-(phenylmethyl)- (9CI) (CA INDEX

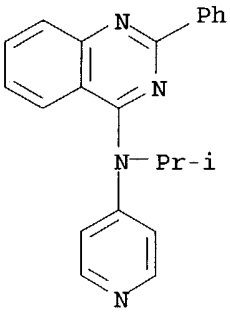
NAME)



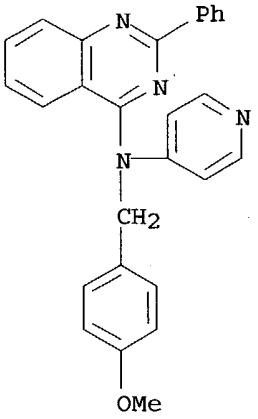
RN 474289-84-4 CAPLUS
CN 4-Quinazolinamine, 2-(3-chlorophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



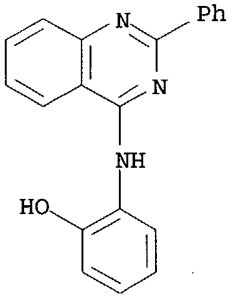
RN 474289-87-7 CAPLUS
CN 4-Quinazolinamine, N-(1-methylethyl)-2-phenyl-N-4-pyridinyl- (9CI) (CA INDEX NAME)



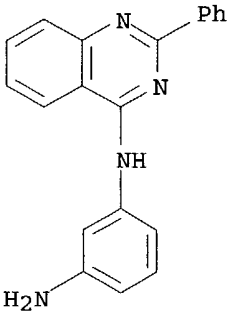
RN 474289-89-9 CAPLUS
CN 4-Quinazolinamine, N-[(4-methoxyphenyl)methyl]-2-phenyl-N-4-pyridinyl- (9CI) (CA INDEX NAME)



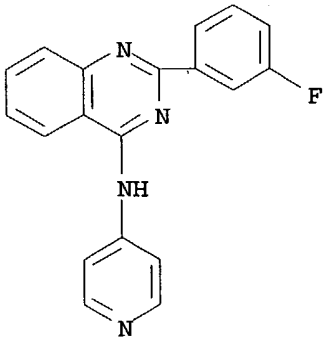
RN 474289-93-5 CAPLUS
CN Phenol, 2-[(2-phenyl-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



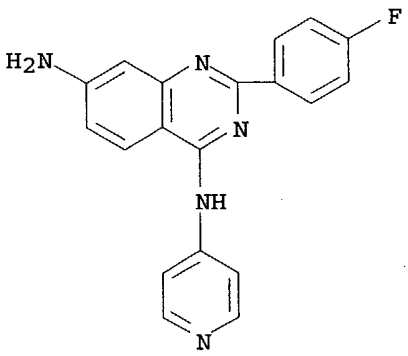
RN 474289-95-7 CAPLUS
CN 1,3-Benzenediamine, N-(2-phenyl-4-quinazolinyl)- (9CI) (CA INDEX NAME)



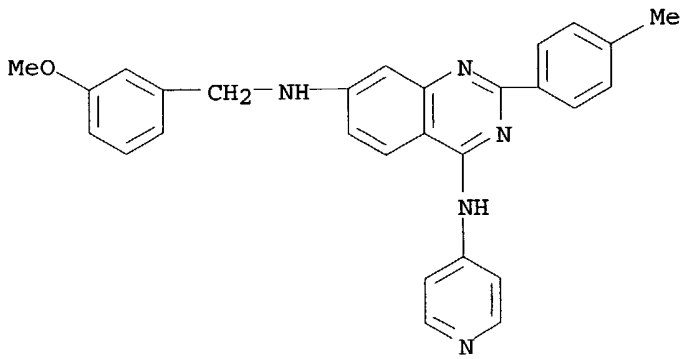
RN 474289-98-0 CAPLUS
CN 4-Quinazolinamine, 2-(3-fluorophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



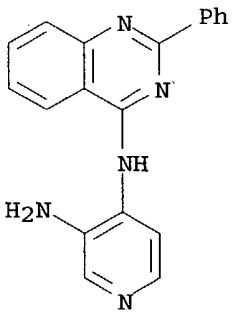
RN 474290-00-1 CAPLUS
CN 4,7-Quinazolinediamine, 2-(4-fluorophenyl)-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



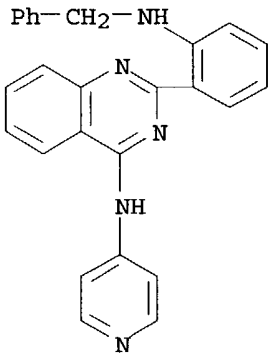
RN 474290-02-3 CAPLUS
CN 4,7-Quinazolinediamine, N7-[(3-methoxyphenyl)methyl]-2-(4-methylphenyl)-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



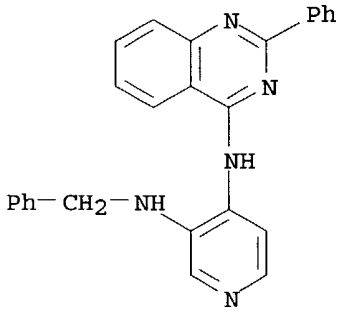
RN 474290-04-5 CAPLUS
CN 3,4-Pyridinediamine, N4-(2-phenyl-4-quinazolinyl)- (9CI) (CA INDEX NAME)



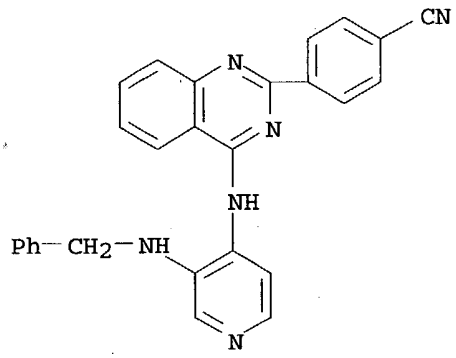
RN 474290-06-7 CAPLUS
CN 4-Quinazolinamine, 2-[2-[(phenylmethyl)amino]phenyl]-N-4-pyridinyl- (9CI) (CA INDEX NAME)



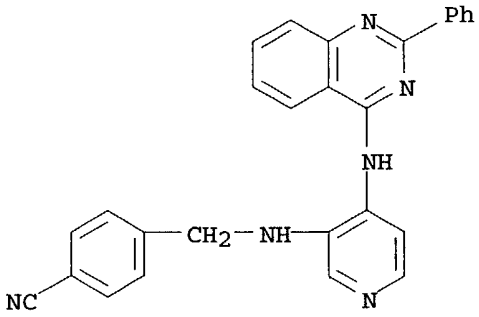
RN 474290-07-8 CAPLUS
CN 3,4-Pyridinediamine, N3-(phenylmethyl)-N4-(2-phenyl-4-quinazolinyl)- (9CI) (CA INDEX NAME)



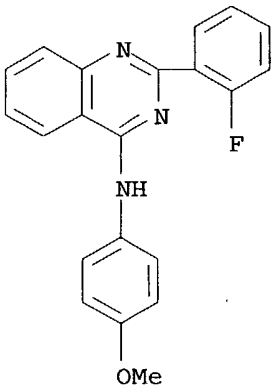
RN 474290-08-9 CAPLUS
CN Benzonitrile, 4-[4-[[3-[(phenylmethyl)amino]-4-pyridinyl]amino]-2-quinazolinyl]- (9CI) (CA INDEX NAME)



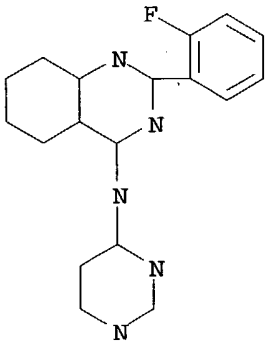
RN 474290-09-0 CAPLUS
CN Benzonitrile, 4-[[[4-[(2-phenyl-4-quinazolinyl)amino]-3-pyridinyl]amino]methyl]- (9CI) (CA INDEX NAME)



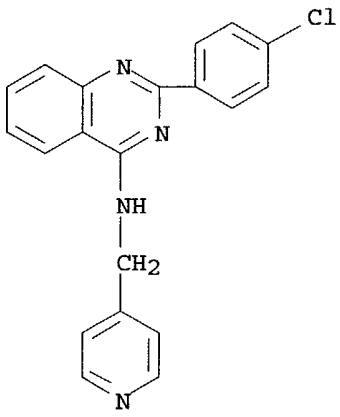
RN 474290-15-8 CAPLUS
CN 4-Quinazolinamine, 2-(2-fluorophenyl)-N-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



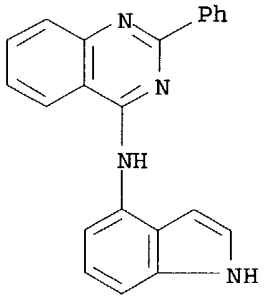
RN 474290-17-0 CAPLUS
CN 4-Quinazolinamine, 2-(2-fluorophenyl)-N-4-pyrimidinyl- (9CI) (CA INDEX NAME)



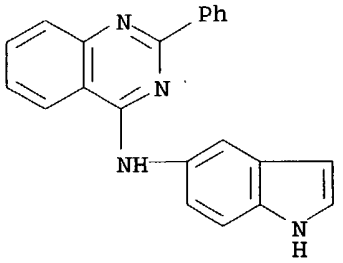
*** FRAGMENT DIAGRAM IS INCOMPLETE ***
RN 474290-19-2 CAPLUS
CN 4-Quinazolinamine, 2-(4-chlorophenyl)-N-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



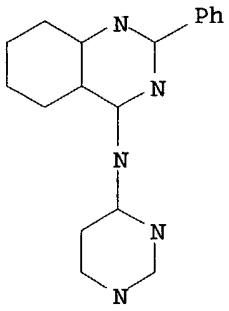
RN 474290-23-8 CAPLUS
CN 4-Quinazolinamine, N-1H-indol-4-yl-2-phenyl- (9CI) (CA INDEX NAME)



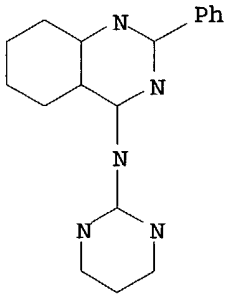
RN 474290-26-1 CAPLUS
CN 4-Quinazolinamine, N-1H-indol-5-yl-2-phenyl- (9CI) (CA INDEX NAME)



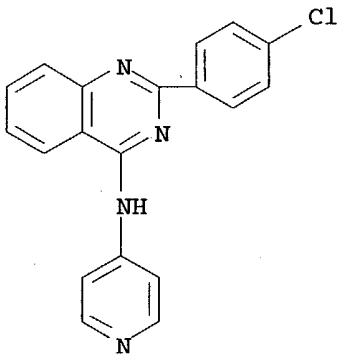
RN 474290-28-3 CAPLUS
CN 4-Quinazolinamine, 2-phenyl-N-4-pyrimidinyl- (9CI) (CA INDEX NAME)



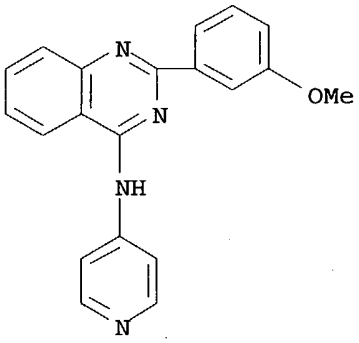
*** FRAGMENT DIAGRAM IS INCOMPLETE ***
RN 474290-30-7 CAPLUS
CN 4-Quinazolinamine, 2-phenyl-N-2-pyrimidinyl- (9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***
RN 474290-32-9 CAPLUS
CN 4-Quinazolinamine, 2-(4-chlorophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



RN 474290-38-5 CAPLUS
CN 4-Quinazolinamine, 2-(3-methoxyphenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



IT **165245-96-5**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibition of **p38-.alpha.**, p38-y and CCK2; prepn. of quinazolines as TGF-.beta. and/or **p38-.alpha. kinase** inhibitors)
RN 165245-96-5 CAPLUS
CN Kinase (phosphorylating), protein, RK (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
REFERENCE COUNT: 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 2 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:121059 CAPLUS
DOCUMENT NUMBER: 140:160157
TITLE: Medium and method for enriching, purifying or depleting ATP binding proteins from a pool of proteins
INVENTOR(S): Godl, Klaus; Missio, Andrea; Daub, Henrik; Stein-Gerlach, Matthias; Greff, Zoltan
PATENT ASSIGNEE(S): Axxima Pharmaceuticals AG, Germany
SOURCE: PCT Int. Appl., 126 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004013633	A2	20040212	WO 2003-EP8375	20030729

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2002-16840 A 20020729
EP 2002-28880 A 20021223

OTHER SOURCE(S): MARPAT 140:160157

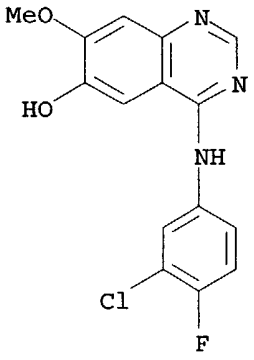
ED Entered STN: 13 Feb 2004

AB The present invention relates to a medium and a method for enriching ATP binding proteins, e.g. proteinkinases, from a pool of proteins, like a proteome. The medium of the present invention comprises specific inhibitors immobilized on a support material. According to the method of the present invention the above-mentioned immobilized compds. are used to selectively bind protein kinases from a pool of heterogeneous proteins.

IT **184475-71-6P 295330-61-9P 655247-74-8P**
655247-75-9P 655247-76-0P 655247-78-2P
RL: ARU (Analytical role, unclassified); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation)
(medium and method for enriching, purifying or depleting ATP binding proteins from pool of proteins)

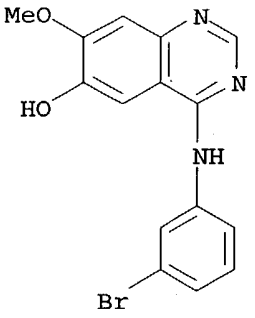
RN 184475-71-6 CAPLUS

CN 6-Quinazolinol, 4-[(3-chloro-4-fluorophenyl)amino]-7-methoxy- (9CI) (CA INDEX NAME)

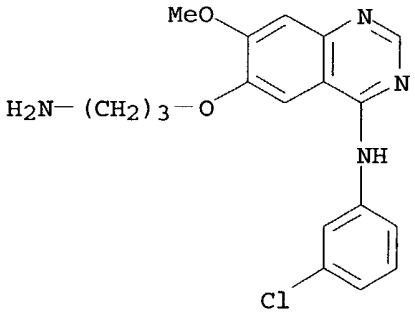


RN 295330-61-9 CAPLUS

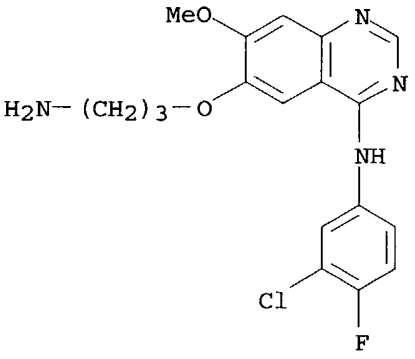
CN 6-Quinazolinol, 4-[(3-bromophenyl)amino]-7-methoxy- (9CI) (CA INDEX NAME)



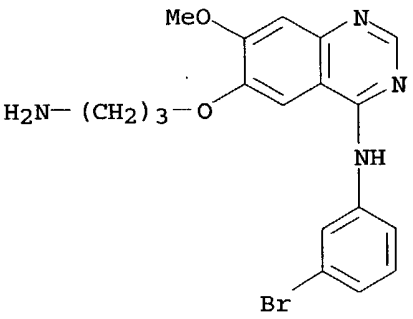
RN 655247-74-8 CAPLUS
CN 4-Quinazolinamine, 6-(3-aminopropoxy)-N-(3-chlorophenyl)-7-methoxy- (9CI) (CA INDEX NAME)



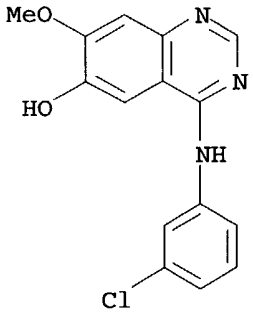
RN 655247-75-9 CAPLUS
CN 4-Quinazolinamine, 6-(3-aminopropoxy)-N-(3-chloro-4-fluorophenyl)-7-methoxy- (9CI) (CA INDEX NAME)



RN 655247-76-0 CAPLUS
CN 4-Quinazolinamine, 6-(3-aminopropoxy)-N-(3-bromophenyl)-7-methoxy- (9CI) (CA INDEX NAME)



RN 655247-78-2 CAPLUS
CN 6-Quinazolinol, 4-[(3-chlorophenyl)amino]-7-methoxy- (9CI) (CA INDEX NAME)



IT **165245-96-5**, p38 MAPK
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(medium and method for enriching, purifying or depleting ATP binding proteins from pool of proteins)
RN 165245-96-5 CAPLUS
CN Kinase (phosphorylating), protein, RK (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L41 ANSWER 3 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:931201 CAPLUS
DOCUMENT NUMBER: 140:13024
TITLE: EGF receptor antagonists in the treatment of gastric cancer
INVENTOR(S): Luber, Birgit; Fuchs, Margit Roswitha; Hoefler, Heinz; Fend, Falko; Gamboa-Dominguez, Armando
PATENT ASSIGNEE(S): Technische Universitaet Muenchen, Germany
SOURCE: PCT Int. Appl., 153 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003097086	A2	20031127	WO 2003-EP5057	20030514
WO 2003097086	A3	20040304		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,
TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ,
MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,
NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-380285P P 20020515
EP 2003-4524 A 20030228

ED Entered STN: 28 Nov 2003

AB The invention relates to a use of (an) EGF receptor antagonist(s)/inhibitor(s) for the prepn. of a pharmaceutical compn. for the prevention, amelioration or treatment of gastric carcinomas, preferably for the prevention, amelioration or treatment of diffuse gastric carcinomas. Furthermore, the invention provides for a method for treating or for preventing gastric carcinomas, in particular diffuse gastric carcinomas comprising the administration of at least one EGF receptor antagonist/inhibitor to a subject in need of such a treatment or prevention.

IT **165245-96-5, p38 Kinase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(EGF receptor antagonists in treatment of gastric cancer)

RN 165245-96-5 CAPLUS

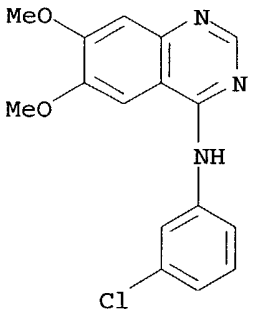
CN Kinase (phosphorylating), protein, RK (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **153436-53-4**, Tyrphostin AG1478 **183319-69-9**, OSI-774
184475-35-2, ZD-1839 **289499-45-2**, CI-1033
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(EGF receptor antagonists in treatment of gastric cancer)

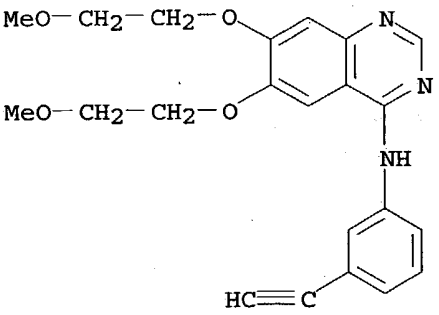
RN 153436-53-4 CAPLUS

CN 4-Quinazolinamine, N-(3-chlorophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



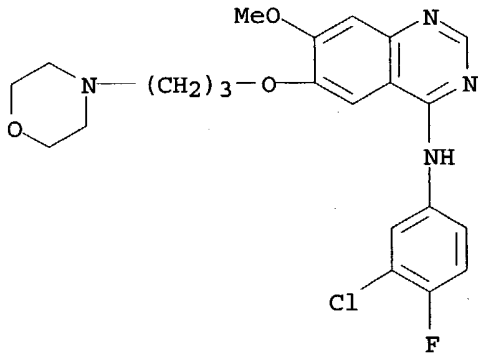
RN 183319-69-9 CAPLUS

CN 4-Quinazolinamine, N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-, monohydrochloride (9CI) (CA INDEX NAME)

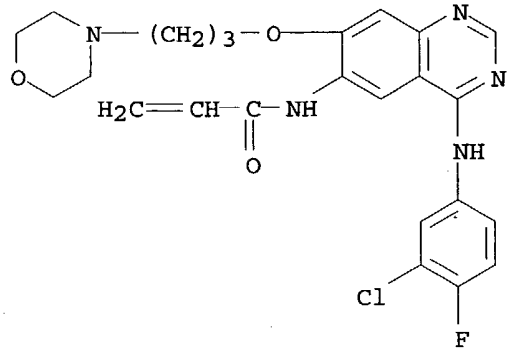


● HCl

RN 184475-35-2 CAPLUS
CN 4-Quinazolinamine, N-(3-chloro-4-fluorophenyl)-7-methoxy-6-[3-(4-morpholinyl)propoxy]- (9CI) (CA INDEX NAME)



RN 289499-45-2 CAPLUS
CN 2-Propenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[3-(4-morpholinyl)propoxy]-6-quinazolinyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

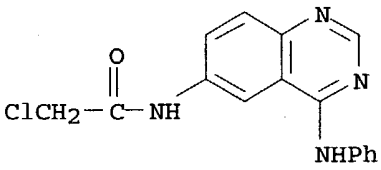
L41 ANSWER 4 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:778056 CAPLUS
DOCUMENT NUMBER: 139:303788
TITLE: Method for identification of kinase inhibitors using covalent tethering of ligands to kinase locked in inactive conformation
INVENTOR(S): Prescott, John C.; Braisted, Andrew
PATENT ASSIGNEE(S): Sunesis Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 260 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003081210	A2	20031002	WO 2003-US8725	20030320
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003232391	A1	20031218	US 2003-394322	20030320

PRIORITY APPLN. INFO.: US 2002-366892P P 20020321
OTHER SOURCE(S): MARPAT 139:303788
ED Entered STN: 03 Oct 2003
AB The invention concerns the identification of protein kinase inhibitors that preferentially bind to the inactive conformation of a target protein kinase. The inhibitors are identified by locking the target protein kinase in an inactive conformation, and using a covalent tethering approach to identify inhibitors preferentially targeting the inactive conformation. This method identifies inhibitors which do not compete directly with ATP for binding to the active conformation of the ATP-binding pocket of the kinase. Thus, using the covalent tethering approach to identify small mol. inhibitors, smaller drug-like fragments (monophores) are first tested for binding activity to kinases which have been modified to contain a tether, or which already contain a tether (a cysteine side-chain SH group, for example). These monophores are then used to synthesize conjugates that bind to non-overlapping sites to generate diaphores that no longer require the tether for binding. Merging of multiple fragments in this way results in a combination of individual binding energies plus a favorable entropic term due to the high local concn. of the second fragment once the first fragment is bound thus yielding ligands having dissocn. consts. in the .mu.M range. This "screen then link" strategy is much more efficient than the traditional approach, allowing a much large survey of chem. diversity space than is achievable using even the largest compd. libraries.
IT **165245-96-5**, Protein kinase RK **608121-96-6**
608121-97-7 608121-98-8 608121-99-9
608122-00-5 608122-01-6 608122-02-7
608122-03-8 608122-04-9 608122-05-0
608122-06-1 608122-07-2 608122-08-3
608122-09-4 608122-10-7 608122-11-8

608122-12-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(method for identification of kinase inhibitors using covalent tethering of ligands to kinase locked in inactive conformation)
RN 165245-96-5 CAPLUS
CN Kinase (phosphorylating), protein, RK (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 608121-96-6 CAPLUS
CN Acetamide, 2-chloro-N-[4-(phenylamino)-6-quinazolinyl]- (9CI) (CA INDEX NAME)



RN 608121-97-7 CAPLUS
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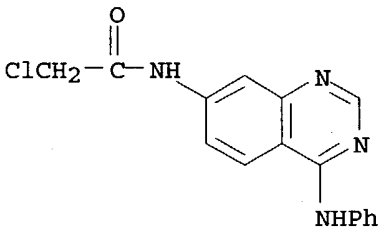
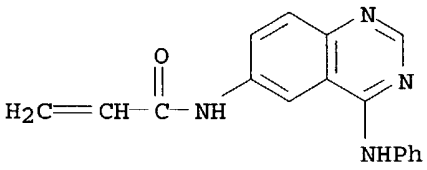


RN 608121-98-8 CAPLUS
CN 2-Propenamide, N-[4-(phenylamino)-6-quinazolinyl]- (9CI) (CA INDEX NAME)



RN 608121-99-9 CAPLUS
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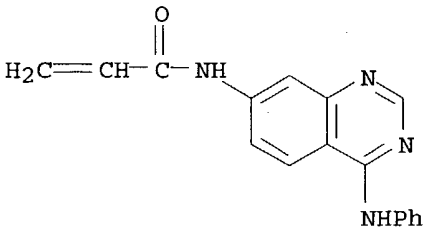
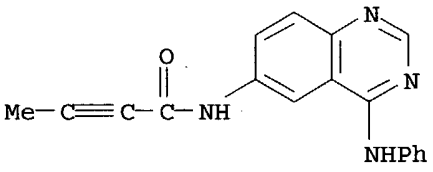
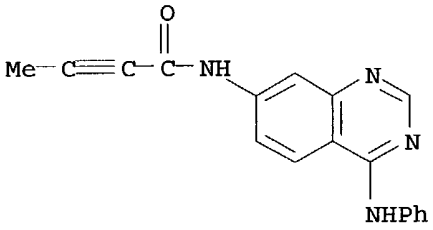


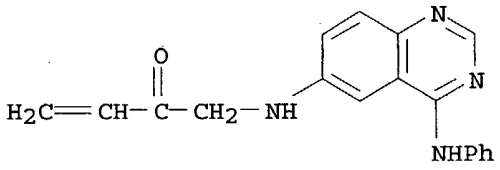
RN 608122-00-5 CAPLUS
CN 2-Butynamide, N-[4-(phenylamino)-6-quinazolinyl]- (9CI) (CA INDEX NAME)



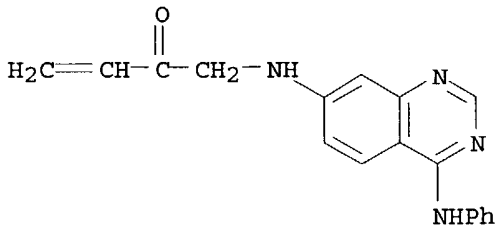
RN 608122-01-6 CAPLUS
CN 2-Butynamide, N-[4-(phenylamino)-7-quinazolinyl]- (9CI) (CA INDEX NAME)



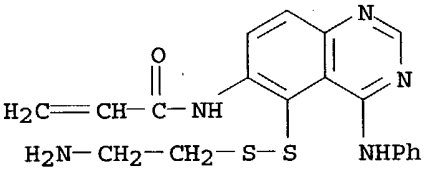
RN 608122-02-7 CAPLUS
CN 3-Buten-2-one, 1-[[4-(phenylamino)-6-quinazolinyl]amino]- (9CI) (CA INDEX NAME)



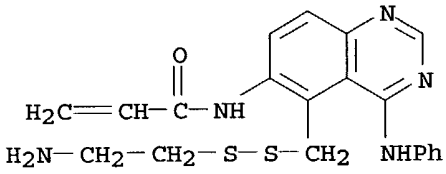
RN 608122-03-8 CAPLUS
CN 3-Buten-2-one, 1-[[4-(phenylamino)-7-quinazolinyl]amino]- (9CI) (CA INDEX NAME)



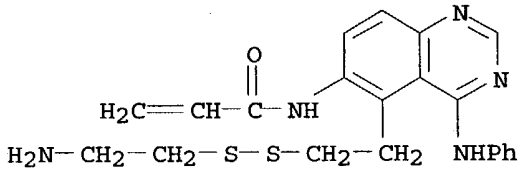
RN 608122-04-9 CAPLUS
CN 2-Propenamide, N-[5-[(2-aminoethyl)dithio]-4-(phenylamino)-6-quinazolinyl]- (9CI) (CA INDEX NAME)



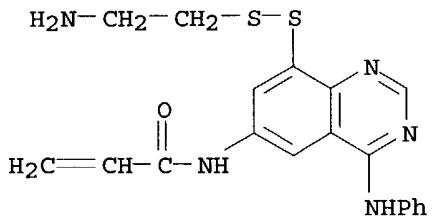
RN 608122-05-0 CAPLUS
CN 2-Propenamide, N-[5-[[(2-aminoethyl)dithio]methyl]-4-(phenylamino)-6-quinazolinyl]- (9CI) (CA INDEX NAME)



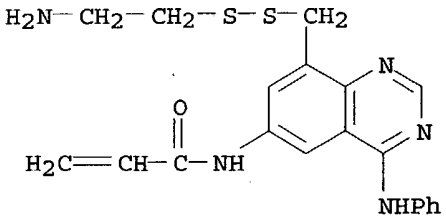
RN 608122-06-1 CAPLUS
CN 2-Propenamide, N-[5-[2-[(2-aminoethyl)dithio]ethyl]-4-(phenylamino)-6-quinazolinyl]- (9CI) (CA INDEX NAME)



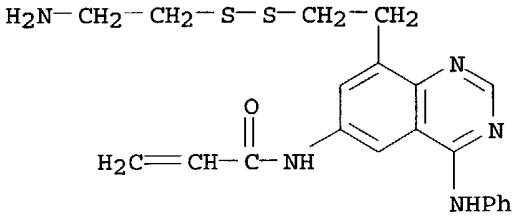
RN 608122-07-2 CAPLUS
CN 2-Propenamide, N-[8-[(2-aminoethyl)dithio]-4-(phenylamino)-6-quinazolinyl]- (9CI) (CA INDEX NAME)



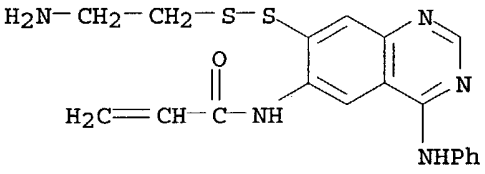
RN 608122-08-3 CAPLUS
CN 2-Propenamide, N-[8-[[(2-aminoethyl)dithio]methyl]-4-(phenylamino)-6-quinazolinyl]- (9CI) (CA INDEX NAME)



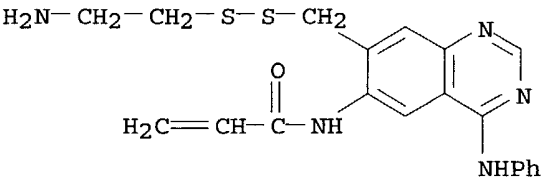
RN 608122-09-4 CAPLUS
CN 2-Propenamide, N-[8-[2-[(2-aminoethyl)dithio]ethyl]-4-(phenylamino)-6-quinazolinyl]- (9CI) (CA INDEX NAME)



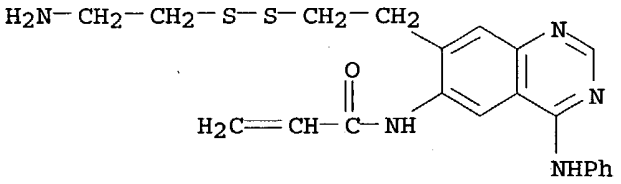
RN 608122-10-7 CAPLUS
CN 2-Propenamide, N-[7-[(2-aminoethyl)dithio]-4-(phenylamino)-6-quinazolinyl]- (9CI) (CA INDEX NAME)



RN 608122-11-8 CAPLUS
CN 2-Propenamide, N-[7-[[(2-aminoethyl)dithio]methyl]-4-(phenylamino)-6-quinazolinyl]- (9CI) (CA INDEX NAME)

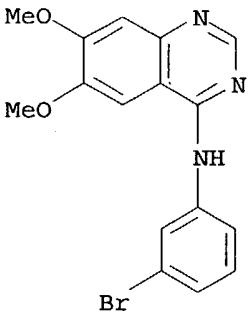


RN 608122-12-9 CAPLUS
CN 2-Propenamide, N-[7-[2-[(2-aminoethyl)dithio]ethyl]-4-(phenylamino)-6-quinazolinyl]- (9CI) (CA INDEX NAME)

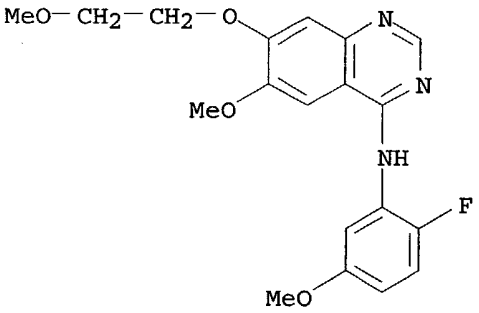


L41 ANSWER 5 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:738968 CAPLUS
DOCUMENT NUMBER: 139:358017
TITLE: Kinases, Homology Models, and High Throughput Docking
AUTHOR(S): Diller, David J.; Li, Rixin
CORPORATE SOURCE: Pharmacopeia, Inc., Princeton, NJ, 08543-5350, USA
SOURCE: Journal of Medicinal Chemistry (2003), 46(22), 4638-4647
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 22 Sep 2003
AB With the many protein sequences coming from the genome sequencing projects, it is unlikely that the authors will ever have an at. resoln. structure of every relevant protein. With high throughput crystallog., however, the authors will soon have representative structures for the vast majority of protein families. Thus the drug discovery and design process will rely heavily on protein modeling to address issues such as designing combinatorial libraries for an entire class of targets and engineering genome-wide selectivity over a target class. In this study the authors assess the value of high throughput docking into homol. models. To do this the authors dock a database of random compds. seeded with known inhibitors into homol. models of six different kinases. In five of the six cases the known inhibitors were enriched by factors of 4-5 in the top 5% of the overall scored and ranked compds. Furthermore, in the same five cases the known inhibitors were enriched by factors of 2-3 in the top 5% of the scored and ranked known kinase inhibitors, thus showing that the homol. models can pick up some of the crucial selectivity information.
IT **165245-96-5, p38 Kinase**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(protein kinases and homol. models and high throughput docking in relation to drug discovery and design)
RN 165245-96-5 CAPLUS
CN Kinase (phosphorylating), protein, RK (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **153436-54-5D**, derivs. **620608-23-3D**, derivs.
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(protein kinases and homol. models and high throughput docking in relation to drug discovery and design)
RN 153436-54-5 CAPLUS
CN 4-Quinazolinamine, N-(3-bromophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



RN 620608-23-3 CAPLUS
CN 4-Quinazolinamine, N-(2-fluoro-5-methoxyphenyl)-6-methoxy-7-(2-methoxyethoxy)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

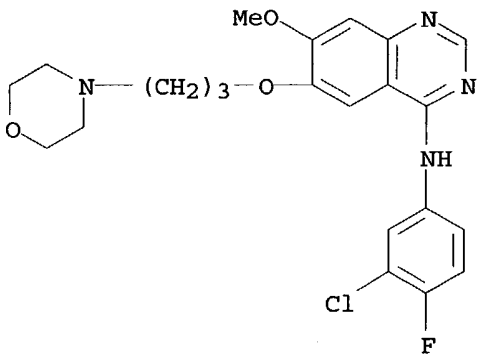
L41 ANSWER 6 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:917378 CAPLUS
DOCUMENT NUMBER: 140:299559
TITLE: Enhancement of tumor radioresponse by combined treatment with gefitinib (Iressa, ZD1839), an epidermal growth factor receptor tyrosine kinase inhibitor, is accompanied by inhibition of DNA damage repair and cell growth in oral cancer
AUTHOR(S): Shintani, Satoru; Li, Chunnan; Mihara, Mariko; Terakado, Nagaaki; Yano, Junya; Nakashiro, Koh-ichi; Hamakawa, Hiroyuki
CORPORATE SOURCE: Department of Oral and Maxillofacial Surgery, Ehime University School of Medicine, Ehime, Japan
SOURCE: International Journal of Cancer (2003), 107(6), 1030-1037
CODEN: IJCNAW; ISSN: 0020-7136
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 24 Nov 2003
AB Mol. blockade of EGFR with either an EGFR MAb or an EGFR TKI enhances the radiosensitivity of human SCCs. In the present study, we investigated whether treatment with the EGFR TKI gefitinib (Iressa, ZD1839) improves the response to radiotherapy in the OSCC cell lines HSC2 and HSC3. We examd. potential mechanisms that may contribute to the enhanced radiation response induced by gefitinib. Growth inhibition was obsd. in vitro with radiation or gefitinib. A cooperative antiproliferative effect was

obtained when cancer cells were treated with radiation followed by gefitinib. Cells treated with a combination of radiation and gefitinib arrested in G1 and G2-M phases, with a decrease in the S-phase population. While radiation alone did not significantly affect MEK1/2 and p38 MAPK autophosphorylation, the combination of gefitinib and radiation completely inhibited the downstream signaling of EGFR. Results from DNA damage repair anal. in cultured OSCC cells demonstrated that gefitinib had a strong inhibitory effect on DNA-PKc pathways after radiation. Tumor xenograft studies demonstrated that the combination of gefitinib and radiation caused growth inhibition and tumor regression of well-established OSCC tumors in athymic mice; tumor vol. was reduced from 1,008.2 to 231.4 mm3 in HSC2 cells ($p < 0.01$) and from 284.2 to 12.4 mm3 in HSC3 cells ($p < 0.01$). Immunohistochem. anal. of OSCC xenografts revealed that gefitinib caused a striking decrease in tumor cell proliferation when combined with radiotherapy. Overall, we conclude that gefitinib enhances tumor radioresponse by multiple mechanisms that may involve antiproliferative growth inhibition and effects on DNA repair after exposure to radiation.

IT **165245-96-5, p38 Kinase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(autophosphorylation; radiotherapy combination with EGFR-TK inhibitor gefitinib: inhibition of DNA damage repair and cell growth in oral cancer)
RN 165245-96-5 CAPLUS
CN Kinase (phosphorylating), protein, RK (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **184475-35-2**, Gefitinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(radiotherapy combination with EGFR-TK inhibitor gefitinib: inhibition of DNA damage repair and cell growth in oral cancer)
RN 184475-35-2 CAPLUS
CN 4-Quinazolinamine, N-(3-chloro-4-fluorophenyl)-7-methoxy-6-[3-(4-morpholinyl)propoxy]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 7 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:98457 CAPLUS
DOCUMENT NUMBER: 139:159425
TITLE: Inhibition of nucleoside transport by protein kinase inhibitors
AUTHOR(S): Huang, Min; Wang, Yanhong; Cogut, Susan B.; Mitchell, Beverly S.; Graves, Lee M.

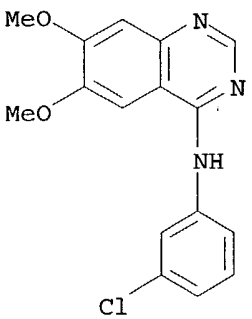
CORPORATE SOURCE: Department of Pharmacology, University of North Carolina, Chapel Hill, NC, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2003), 304(2), 753-760
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 09 Feb 2003

AB Recently we reported that the pyridinylimidazole class of p38 mitogen-activated protein (MAP) kinase inhibitors potently inhibited the facilitated transport of nucleosides and nucleoside analogs in K562 cells. These compds. competed with the binding of nitrobenzylthioinosine (NBMPR) to K562 cells, consistent with inhibition of the NBMPR-sensitive equilibrative transporter (ENT1). In this study we examd. a large no. of addnl. protein kinase inhibitors for their effects on nucleoside transport. We find that incubation of K562 cells with tyrosine kinase inhibitors (AG825, AG1517, AG1478, STI-571), protein kinase C (PKC) inhibitors (stauro-sporine, GF 109203X, RO 31-8220, arcyriarubin A), cyclin-dependent kinase inhibitors (roscovitine, olomoucine, indirubin-3'-monoxime), or rapamycin resulted in a dose-dependent redn. of intracellular uptake of [3H]uridine. In contrast, neither the MAP kinase kinase inhibitors (U0126, PD 98059) nor the phosphatidyl inositol-3 kinase inhibitors (wortmannin, LY 294002) affected this process. Furthermore, both transient uptake and prolonged [3H]thymidine incorporation in K562 cells were inhibited by protein kinase inhibitors, inactive analogs of kinase inhibitors (RO 31-6045, SB202474), and NBMPR, independently of effects on cell proliferation as detd. by MTT assay. These studies demonstrate that a wide variety of protein kinase inhibitors affect nucleoside uptake through selective inhibition of nucleoside transporters, independently of kinase inhibition.

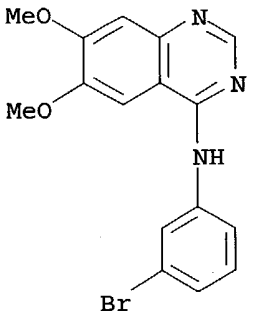
IT **165245-96-5, p38 Kinase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; protein **kinase** inhibitors structure-related inhibition of nucleoside transport)
RN 165245-96-5 CAPLUS
CN Kinase (phosphorylating), protein, RK (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **153436-53-4**, AG1478 **153436-54-5**, AG 1517
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protein kinase inhibitors structure-related inhibition of nucleoside transport)
RN 153436-53-4 CAPLUS
CN 4-Quinazolinamine, N-(3-chlorophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



RN 153436-54-5 CAPLUS
CN 4-Quinazolinamine, N-(3-bromophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 8 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:615388 CAPLUS
DOCUMENT NUMBER: 137:150239
TITLE: Cyclic GMP- and protein kinase G-based method of treating conditions related to platelet activity
INVENTOR(S): Du, Xiaoping
PATENT ASSIGNEE(S): The Board of Trustees of the University of Illinois, USA
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

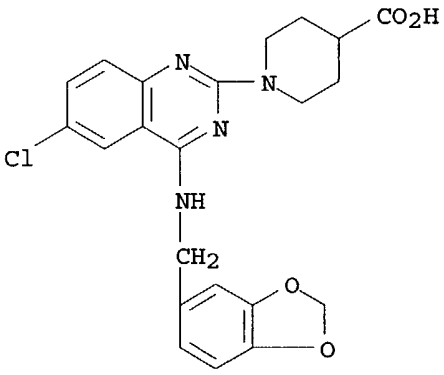
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002062325	A2	20020815	WO 2002-US3372	20020205
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004087539	A1	20040506	US 2003-467387	20031212

PRIORITY APPLN. INFO.: US 2001-267326P P 20010208
WO 2002-US3372 W 20020205

ED Entered STN: 16 Aug 2002
AB Methods of treating thrombotic and hemostatic conditions related to platelet activity are described. The methods of treating thrombotic and hemostatic conditions use active agents that modulate prodn. of guanosine 3', 5' cyclic monophosphate (cGMP) or the function of cGMP-dependent protein kinase (PKG), and its downstream effectors, the ERK and p38 pathways.
IT **165245-96-5, p38 Kinase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cyclic GMP- and protein kinase G-based method of treating conditions

related to platelet activity)
RN 165245-96-5 CAPLUS
CN Kinase (phosphorylating), protein, RK (9CI) (CA INDEX NAME)

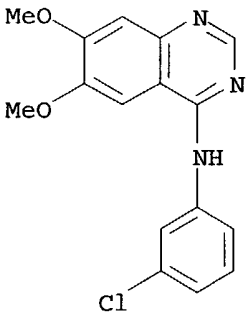
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **150452-19-0**, E4021
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclic GMP- and protein kinase G-based method of treating conditions related to platelet activity)
RN 150452-19-0 CAPLUS
CN 4-Piperidinecarboxylic acid, 1-[4-[(1,3-benzodioxol-5-ylmethyl)amino]-6-chloro-2-quinazolinyl]-, monosodium salt (9CI) (CA INDEX NAME)



L41 ANSWER 9 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:523279 CAPLUS
DOCUMENT NUMBER: 137:242433
TITLE: Vitamin D inhibits the activation of stress-activated protein kinases by physiological and environmental stresses in keratinocytes
AUTHOR(S): Ravid, A.; Rubinstein, E.; Gamady, A.; Rotem, C.; Liberman, U. A.; Koren, R.
CORPORATE SOURCE: Basil and Gerald Felsenstein Medical Research Center, Sackler Faculty of Medicine, Tel Aviv University, Petah Tikva, 49100, Israel
SOURCE: Journal of Endocrinology (2002), 173(3), 525-532
CODEN: JOENAK; ISSN: 0022-0795
PUBLISHER: Society for Endocrinology
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 14 Jul 2002
AB In addn. to its known effects on keratinocyte proliferation and differentiation, the hormonal form of vitamin D, 1,25-dihydroxyvitamin D3 (1,25(OH)2D3), has been shown to protect keratinocytes from UV- and chemotherapy-induced damage. Epidermal keratinocytes contain both the machinery needed to produce 1,25(OH)2D3 and vitamin D receptors. The activation of the stress-activated protein kinases (SAPKs), such as c-Jun N-terminal kinase (JNK) and p38, is an early cellular response to stress signals and an important determinant of cell fate. This study examines whether modulation of these SAPKs is assocd. with the effects of

1,25(OH)2D3 on keratinocytes under stress. HaCaT keratinocytes were exposed to heat shock, hyperosmotic concns. of sorbitol, the epidermal growth factor receptor tyrosine kinase inhibitor AG1487, the pro-inflammatory cytokine tumor necrosis factor .alpha., and H2O2. These stresses activated both SAPKs. Pretreatment with 1,25(OH)2D3 inhibited the activation of JNK by all stresses and the activation of p38 by heat shock, AG1478 and tumor necrosis factor .alpha.. Under the same conditions, treatment with 1,25(OH)2D3 protected HaCaT keratinocytes from cytotoxicity induced by exposure to H2O2 and hyperosmotic shock. The effect of 1,25(OH)2D3 was dose-dependent, already apparent at nanomolar concns., and time-dependent, maximal after a 24-h pre-incubation. We suggest that inhibition of SAPK activation may account for some of the well-documented protective effects of 1,25(OH)2D3 on epidermal cells during exposure to UV or chemotherapy and may also be related to the anti-inflammatory actions of the hormone in skin.

IT **153436-53-4**, Tyrphostin AG 1478
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (stressor; vitamin D inhibits activation of stress-activated protein kinases by physiol. and environmental stresses in keratinocytes)
RN 153436-53-4 CAPLUS
CN 4-Quinazolinamine, N-(3-chlorophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)

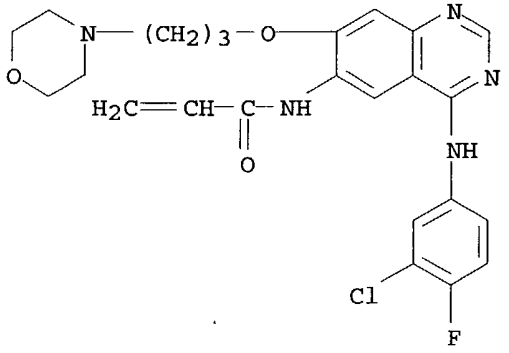


IT **165245-96-5**, **p38** Mitogen-activated protein **kinase**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (vitamin D inhibits activation of stress-activated protein kinases by physiol. and environmental stresses in keratinocytes)
RN 165245-96-5 CAPLUS
CN Kinase (phosphorylating), protein, RK (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 10 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:367797 CAPLUS
DOCUMENT NUMBER: 135:102151
TITLE: Akt, MAPK (Erk1/2), and p38 act in concert to promote apoptosis in response to ErbB receptor family inhibition
AUTHOR(S): Nelson, James M.; Fry, David W.
CORPORATE SOURCE: Pfizer Global Research and Development, Ann Arbor, MI, 48105, USA
SOURCE: Journal of Biological Chemistry (2001), 276(18), 14842-14847
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular

Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 23 May 2001
AB The ErbB receptor family is implicated in the malignant transformation of several tumor types and is over-expressed frequently in breast, ovarian, and other tumors. The mechanism by which CI-1033 and gemcitabine, either singly or in combination, kill tumor cells was examd. in two breast lines, MDA-MB-453 and BT474; both overexpress the ErbB-2 receptor. CI-1033, a potent inhibitor of the ErbB family of receptor tyrosine kinases, reduced levels of activated Akt in MDA-MB-453 cells. This effect alone, however, did not induce apoptosis in these cells. Gemcitabine treatment resulted in a moderate increase in the percentage of apoptotic cells that was accompanied by activation of p38 and MAPK (ERK1/2). CI-1033 given 24 h after gemcitabine produced a significant increase in the apoptotic fraction over treatment with either drug alone. During the combined treatment p38 remained activated, whereas Akt and activated MAPK were suppressed. Substitution of CI-1033 with the phosphatidylinositol 3-kinase inhibitor LY294002 and the MAPK/ERK kinase inhibitor PD098059 in combination with gemcitabine produced the same results as the combination of CI-1033 and gemcitabine. P38 suppression by SB203580 prevented the enhanced cell kill by CI-1033. In contrast to MDA-MB-453, BT474 cells exhibited activated p38 under unstressed conditions as well as activated Akt and MAPK. Treatment of BT474 cells with CI-1033 inhibited both the phosphorylation of Akt and MAPK and resulted in a 47% apoptotic fraction. Gemcitabine did not cause apoptosis in the BT474 cells. These data indicate that suppression of Akt and MAPK in the presence of activated p38 results in cell death and a possible mechanism for the enhanced apoptosis produced by the combination of CI-1033 and gemcitabine in MDA-MB-453 cells. Furthermore, tumors that depend on ErbB receptor signaling for survival and exhibit activated p38 in the basal state may be susceptible to apoptosis by CI-1033 as a single agent.
IT **267243-28-7**, CI-1033
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(Akt, MAPK (Erk1/2), and p38 act in concert to promote apoptosis in human breast carcinoma in response to ErbB receptor family inhibition)
RN 267243-28-7 CAPLUS
CN 2-Propenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[3-(4-morpholinyl)propoxy]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



IT **165245-96-5, p38 kinase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(Akt, MAPK (Erk1/2), and p38 act in concert to promote apoptosis in human breast carcinoma in response to ErbB receptor family inhibition)

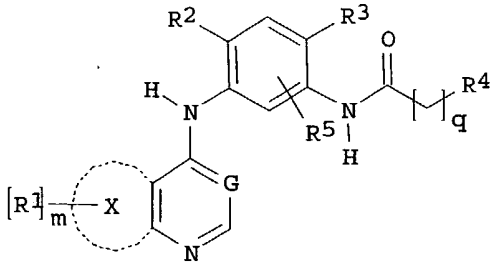
RN 165245-96-5 CAPLUS
CN Kinase (phosphorylating), protein, RK (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 11 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:688241 CAPLUS
DOCUMENT NUMBER: 133:252455
TITLE: Preparation of pyridine and pyrimidine derivatives as inhibitors of cytokine mediated disease
INVENTOR(S): Cumming, John Graham
PATENT ASSIGNEE(S): Astrazeneca Ab, Swed.
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000056738	A1	20000928	WO 2000-GB1006	20000317
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000009223	A	20011226	BR 2000-9223	20000317
EP 1165566	A1	20020102	EP 2000-912750	20000317
EP 1165566	B1	20030820		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002540112	T2	20021126	JP 2000-606599	20000317
AU 757028	B2	20030130	AU 2000-34401	20000317
AU 2000034401	A5	20001009		
AT 247661	E	20030915	AT 2000-912750	20000317
NZ 514042	A	20031031	NZ 2000-514042	20000317
PT 1165566	T	20040130	PT 2000-912750	20000317
ZA 2001007501	A	20021211	ZA 2001-7501	20010911
NO 2001004589	A	20011121	NO 2001-4589	20010921

PRIORITY APPLN. INFO.: GB 1999-6566 A 19990323
WO 2000-GB1006 W 20000317
OTHER SOURCE(S): MARPAT 133:252455
ED Entered STN: 29 Sep 2000
GI



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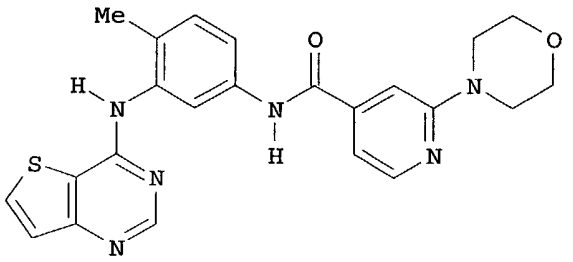


II

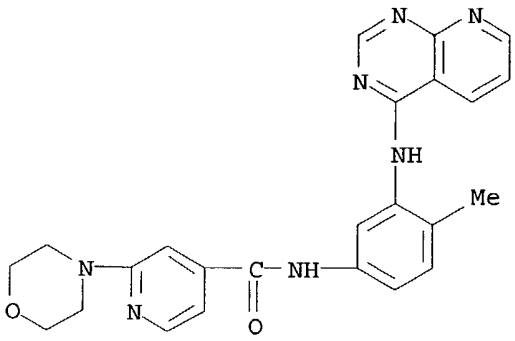
AB The title compds. [I; G = N, CH, C(CN); ring X = a 5-6 membered fused heteroaryl ring which contains 1-3 heteroatoms selected from O, S and N; m = 0-2; R1 = OH, halo, CF3, etc.; R2, R3 = H, halo, alkyl, etc.; R4 = H, OH, alkyl, etc.; R5 = H, halo, CF3, etc.; q = 0-4], useful in the treatment of diseases or medical conditions mediated by cytokines, were prepd. and formulated. E.g., a multi-step synthesis of thieno[3,2-d]pyrimidine II which showed IC50 of 0.06 against p38.alpha., was given.

IT **295776-76-0P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of pyridine and pyrimidine derivs. as inhibitors of cytokine mediated disease)

RN 295776-76-0 CAPLUS

CN 4-Pyridinecarboxamide, N-[4-methyl-3-(pyrido[2,3-d]pyrimidin-4-ylamino)phenyl]-2-(4-morpholinyl)- (9CI) (CA INDEX NAME)



IT **165245-96-5, p38 Kinase**

RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(prepn. of pyridine and pyrimidine derivs. as inhibitors of cytokine mediated disease)
RN 165245-96-5 CAPLUS
CN Kinase (phosphorylating), protein, RK (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 12 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:535166 CAPLUS
DOCUMENT NUMBER: 133:129859
TITLE: Inhibition of STAT3 signal transduction and the treatment of cancer in humans
INVENTOR(S): Jove, Richard; Dalton, William; Sebti, Said; Yu, Hua; Heller, Richard; Jaroszeski, Mark
PATENT ASSIGNEE(S): University of South Florida, USA
SOURCE: PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

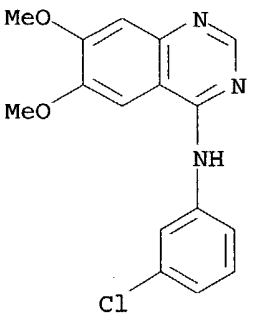
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000044774	A2	20000803	WO 2000-US1845	20000127
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1146869	A2	20011024	EP 2000-905724	20000127
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2003525862	T2	20030902	JP 2000-596030	20000127

PRIORITY APPLN. INFO.: US 1999-117600P P 19990127
WO 2000-US1845 W 20000127

ED Entered STN: 04 Aug 2000
AB Signal Transducer and Activator of Transcription (STAT) proteins have a fundamental role cell signaling, and are activated by a large no. of cytokines and growth factors. One member of the STAT family, STAT3, has a crit. role in oncogenesis. The present invention relates generally to disruption of the pathway of STAT3 signaling in the treatment of human cancer. STAT3 activation is shown to be present in diverse tumor cell lines and tumors, to promote oncogenesis, to inhibit apoptosis, and to reduce sensitivity to chemotherapeutic agents. Inhibition of STAT3 signaling induces apoptosis specifically in tumor cell lines, and increases sensitivity to chemotherapeutic agents. The invention relates more particularly to methods, compns., means of administering such compns., and means for identifying such compns. for the inhibition of STAT3 intracellular signaling in the treatment of human cancers. Activation of STAT3, as measured EMSA, was inhibted in tumor cell lines by inhibitors of Src and Jak protein tyrosine kinases. The Jak kinase inhibitor AG490 blocked the proliferation of human mammary tumors in nude mice. Blocking of serine phosphorylation of STAT3 had similar effects.

IT **165245-96-5, p38 Kinase**
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PROC (Process); USES (Uses)
(STAT3 activation by, in tumor cell lines; inhibition of STAT3 signal transduction and treatment of cancer in humans)
RN 165245-96-5 CAPLUS
CN Kinase (phosphorylating), protein, RK (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **153436-53-4**, AG 1478
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of STAT3 activation by, in tumor cell lines; inhibition of STAT3 signal transduction and treatment of cancer in humans)
RN 153436-53-4 CAPLUS
CN 4-Quinazolinamine, N-(3-chlorophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



L41 ANSWER 13 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:241203 CAPLUS
DOCUMENT NUMBER: 132:265207
TITLE: Preparation of 4-anilinoquinazolines and 4-anilinoquinolines as inhibitors of cytokine mediated disease
INVENTOR(S): Cumming, John Graham
PATENT ASSIGNEE(S): Zeneca Limited, UK
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000020402	A1	20000413	WO 1999-GB3220	19990927

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,

CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2341374	AA	20000413	CA 1999-2341374	19990927
AU 9961064	A1	20000426	AU 1999-61064	19990927
AU 761552	B2	20030605		
BR 9914162	A	20010626	BR 1999-14162	19990927
EP 1117653	A1	20010725	EP 1999-947686	19990927
EP 1117653	B1	20030205		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002526538	T2	20020820	JP 2000-574519	19990927
AT 232205	E	20030215	AT 1999-947686	19990927
NZ 510210	A	20030630	NZ 1999-510210	19990927
PT 1117653	T	20030630	PT 1999-947686	19990927
ES 2191462	T3	20030901	ES 1999-947686	19990927
ZA 2001002187	A	20020618	ZA 2001-2187	20010315
US 6593333	B1	20030715	US 2001-787883	20010323
NO 2001001631	A	20010521	NO 2001-1631	20010330
HK 1037367	A1	20030822	HK 2001-108138	20011119
US 2003216417	A1	20031120	US 2003-441084	20030520
US 6716847	B2	20040406		

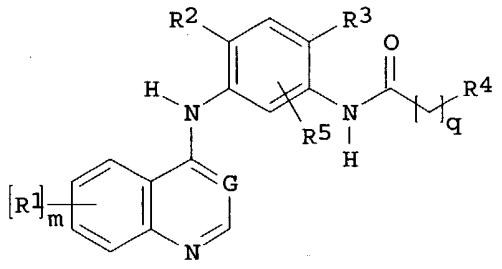
PRIORITY APPLN. INFO.:

GB 1998-21338	A	19981001
GB 1999-6564	A	19990323
WO 1999-GB3220	W	19990927
US 2001-787883	A3	20010323

OTHER SOURCE(S): MARPAT 132:265207

ED Entered STN: 14 Apr 2000

GI



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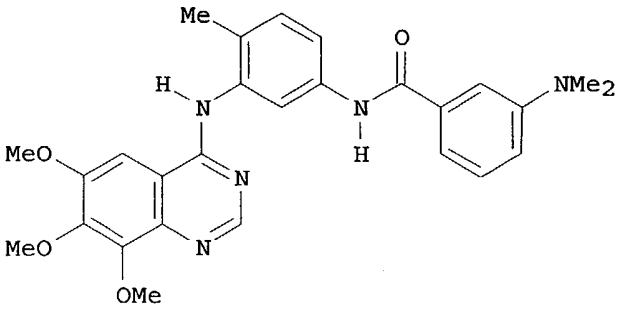


II

AB The title compds. [I; G = N, CH; R1 = OH, halo, CF3, etc.; R2, R3 = H, halo, alkyl, etc.; R4 = H, OH, alkyl, etc.; R5 = H, halo, CF3; m = 1-3; q = 0-4] and their pharmaceutically acceptable salts or in vivo cleavable esters, useful in the treatment of diseases or medical conditions mediated

by cytokines, were prepd. and formulated. E.g., a multi-step synthesis of II which showed IC50 of 0.2 .mu.M against p38.alpha. kinase and IC50 of 5.2 .mu.M against TNF.alpha. prodn., was given.

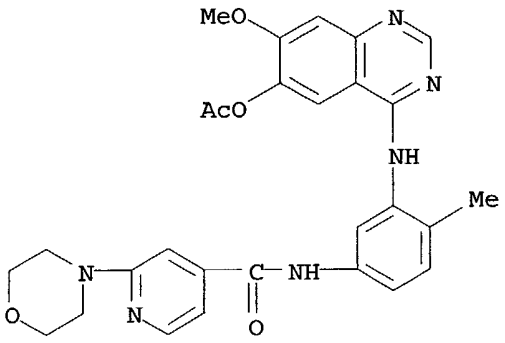
IT **263400-17-5P 263400-18-6P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(prepn. of 4-anilinoquinazolines and 4-anilinoquinolines as inhibitors of cytokine mediated disease)

RN 263400-17-5 CAPLUS

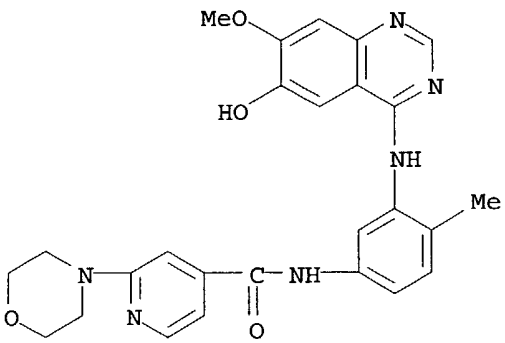
CN 4-Pyridinecarboxamide, N-[3-[[6-(acetyloxy)-7-methoxy-4-quinazolinyl]amino]-4-methylphenyl]-2-(4-morpholinyl)-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 263400-18-6 CAPLUS

CN 4-Pyridinecarboxamide, N-[3-[(6-hydroxy-7-methoxy-4-quinazolinyl)amino]-4-methylphenyl]-2-(4-morpholinyl)- (9CI) (CA INDEX NAME)



IT **263399-67-3P 263399-68-4P 263399-70-8P**
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263399-78-6P 263399-79-7P 263399-80-0P
263399-81-1P 263399-82-2P 263399-83-3P
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263400-09-5P 263400-10-8P 263400-11-9P
263400-12-0P 263400-13-1P 263400-19-7P
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263400-23-3P 263400-25-5P 263400-26-6P
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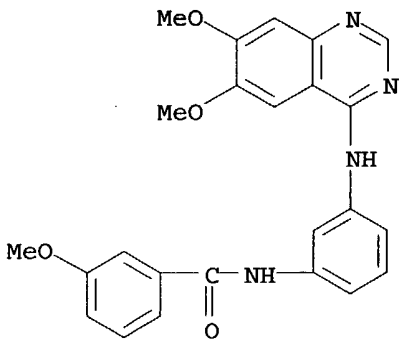
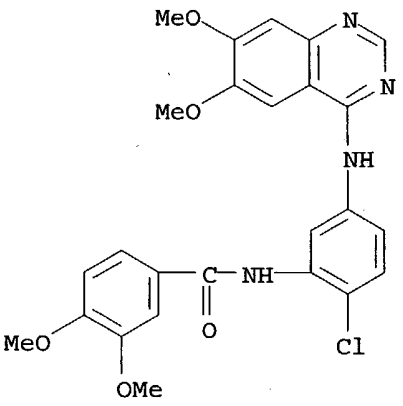
263400-30-2P 263400-31-3P 263400-32-4P
263400-33-5P 263400-34-6P 263400-35-7P
263400-36-8P 263400-37-9P 263400-38-0P
263400-39-1P 263400-40-4P 263400-41-5P
263400-42-6P 263400-43-7P 263400-44-8P
263400-45-9P 263400-46-0P 263400-48-2P
263400-50-6P 263400-51-7P 263400-52-8P
263400-53-9P 263400-94-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 4-anilinoquinazolines and 4-anilinoquinolines as inhibitors of cytokine mediated disease)

RN 263399-67-3 CAPLUS
CN Benzamide, N-[3-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-3-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)



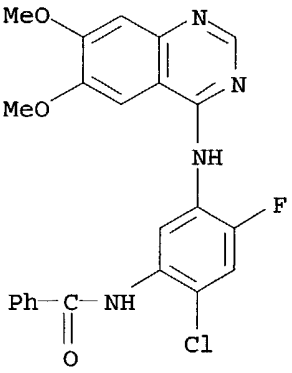
● HCl

RN 263399-68-4 CAPLUS
CN Benzamide, N-[2-chloro-5-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-3,4-dimethoxy-, monohydrochloride (9CI) (CA INDEX NAME)



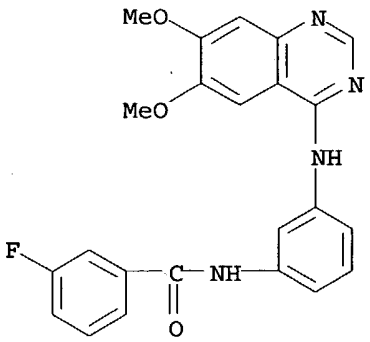
● HCl

RN 263399-70-8 CAPLUS
CN Benzamide, N-[2-chloro-5-[(6,7-dimethoxy-4-quinazolinyl)amino]-4-fluorophenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



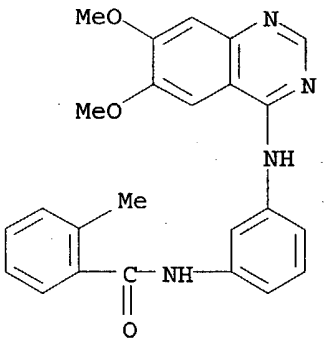
● HCl

RN 263399-71-9 CAPLUS
CN Benzamide, N-[3-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-3-fluoro-, monohydrochloride (9CI) (CA INDEX NAME)



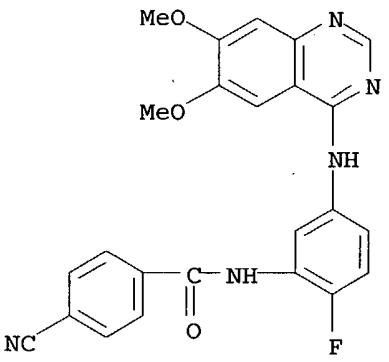
● HCl

RN 263399-72-0 CAPLUS
CN Benzamide, N-[3-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)



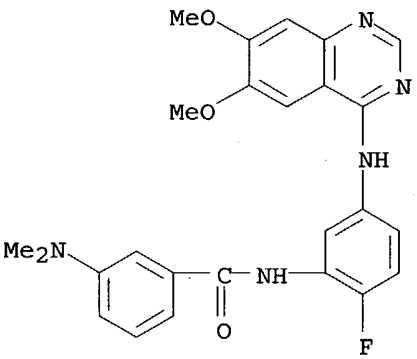
● HCl

RN 263399-74-2 CAPLUS
CN Benzamide, 4-cyano-N-[5-[(6,7-dimethoxy-4-quinazolinyl)amino]-2-fluorophenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



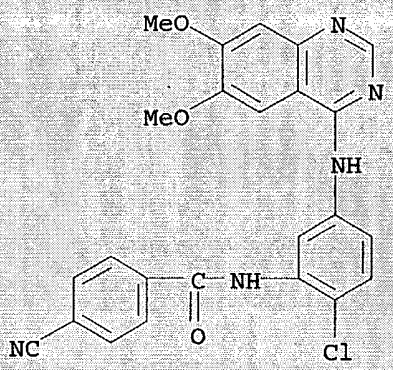
● HCl

RN 263399-75-3 CAPLUS
CN Benzamide, N-[5-[(6,7-dimethoxy-4-quinazolinyl)amino]-2-fluorophenyl]-3-(dimethylamino)-, dihydrochloride (9CI) (CA INDEX NAME)



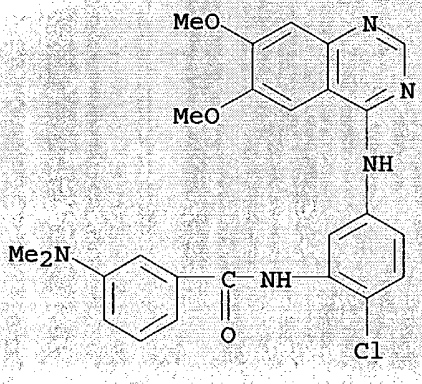
●2 HCl

RN 263399-76-4 CAPLUS
CN Benzamide, N-[2-chloro-5-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-4-cyano-, monohydrochloride (9CI) (CA INDEX NAME)



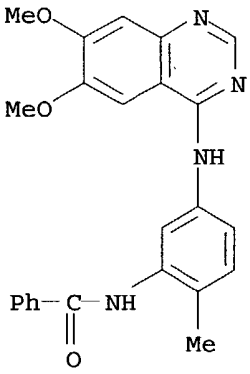
● HCl

RN 263399-77-5 CAPLUS
CN Benzamide, N-[2-chloro-5-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-3-(dimethylamino)-, dihydrochloride (9CI) (CA INDEX NAME)



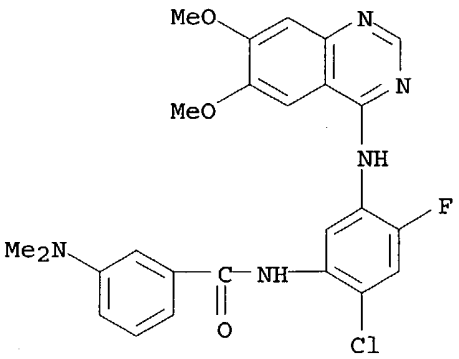
●2 HCl

RN 263399-78-6 CAPLUS
CN Benzamide, N-[5-[(6,7-dimethoxy-4-quinazolinyl)amino]-2-methylphenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



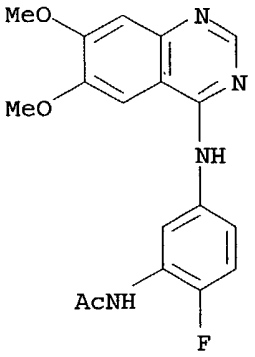
● HCl

RN 263399-79-7 CAPLUS
CN Benzamide, N-[2-chloro-5-[(6,7-dimethoxy-4-quinazolinyl)amino]-4-fluorophenyl]-3-(dimethylamino)-, dihydrochloride (9CI) (CA INDEX NAME)



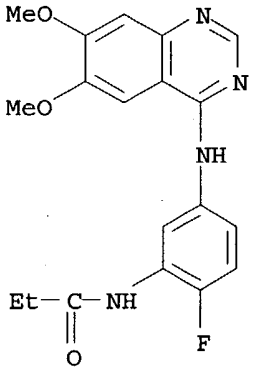
●2 HCl

RN 263399-80-0 CAPLUS
CN Acetamide, N-[5-[(6,7-dimethoxy-4-quinazolinyl)amino]-2-fluorophenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



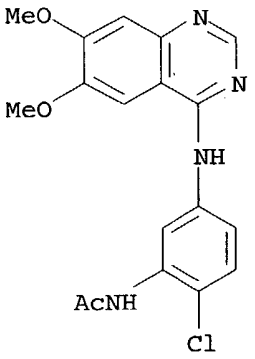
● HCl

RN 263399-81-1 CAPLUS
CN Propanamide, N-[5-[(6,7-dimethoxy-4-quinazolinyl)amino]-2-fluorophenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



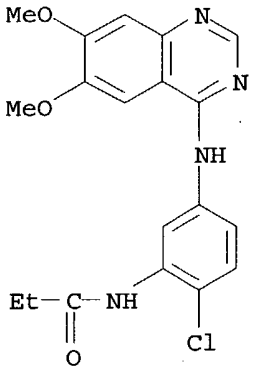
● HCl

RN 263399-82-2 CAPLUS
CN Acetamide, N-[2-chloro-5-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



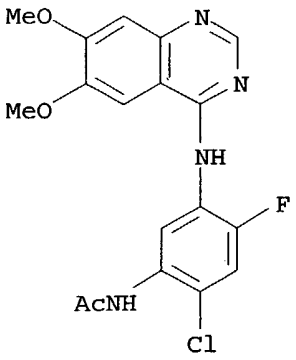
● HCl

RN 263399-83-3 CAPLUS
CN Propanamide, N-[2-chloro-5-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



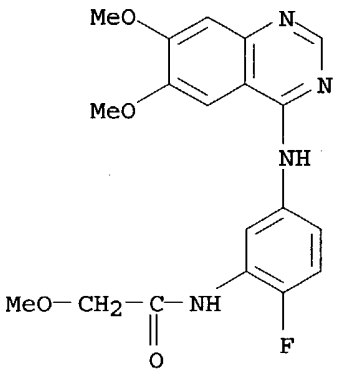
● HCl

RN 263399-84-4 CAPLUS
CN Acetamide, N-[2-chloro-5-[(6,7-dimethoxy-4-quinazolinyl)amino]-4-fluorophenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



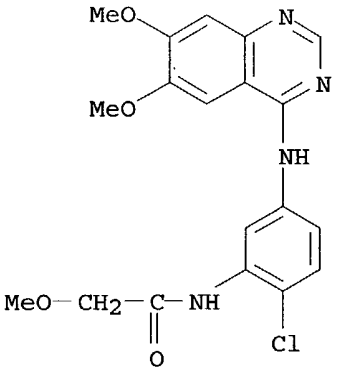
● HCl

RN 263399-85-5 CAPLUS
CN Acetamide, N-[5-[(6,7-dimethoxy-4-quinazolinyl)amino]-2-fluorophenyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)



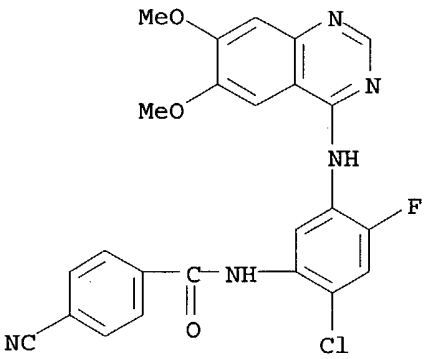
● HCl

RN 263399-86-6 CAPLUS
CN Acetamide, N-[2-chloro-5-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)



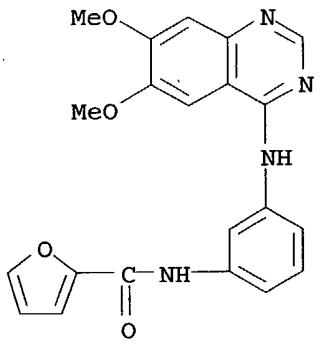
● HCl

RN 263399-87-7 CAPLUS
CN Benzamide, N-[2-chloro-5-[(6,7-dimethoxy-4-quinazolinyl)amino]-4-fluorophenyl]-4-cyano-, monohydrochloride (9CI) (CA INDEX NAME)



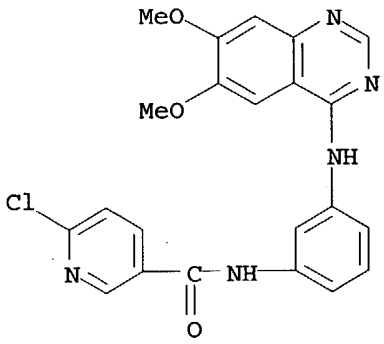
● HCl

RN 263399-88-8 CAPLUS
CN 2-Furancarboxamide, N-[3-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



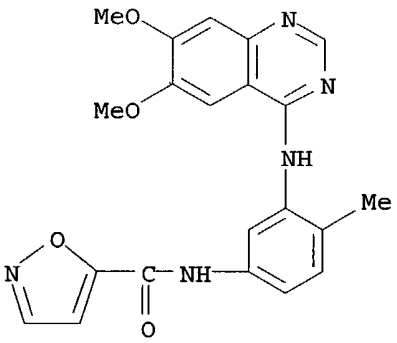
● HCl

RN 263399-89-9 CAPLUS
CN 3-Pyridinecarboxamide, 6-chloro-N-[3-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



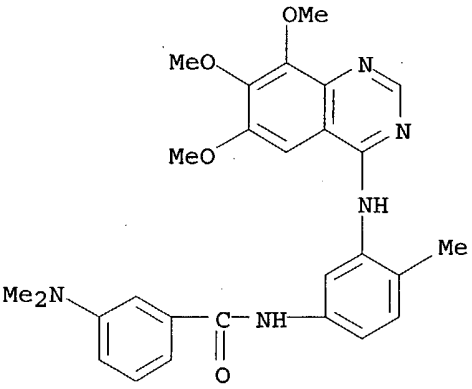
● HCl

RN 263399-90-2 CAPLUS
CN 5-Isoxazolecarboxamide, N-[3-[(6,7-dimethoxy-4-quinazolinyl)amino]-4-methylphenyl]-, monohydrochloride (9CI) (CA INDEX NAME)

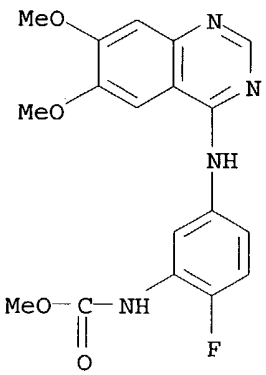


● HCl

RN 263399-91-3 CAPLUS
CN Benzamide, 3-(dimethylamino)-N-[4-methyl-3-[(6,7,8-trimethoxy-4-quinazolinyl)amino]phenyl]- (9CI) (CA INDEX NAME)

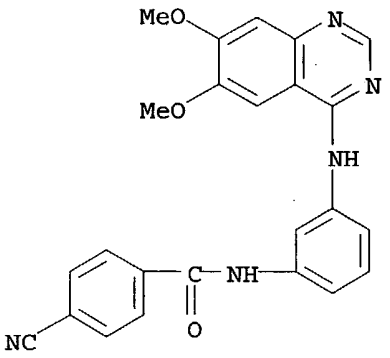


RN 263399-92-4 CAPLUS
CN Carbamic acid, [5-[(6,7-dimethoxy-4-quinazolinyl)amino]-2-fluorophenyl]-, methyl ester (9CI) (CA INDEX NAME)



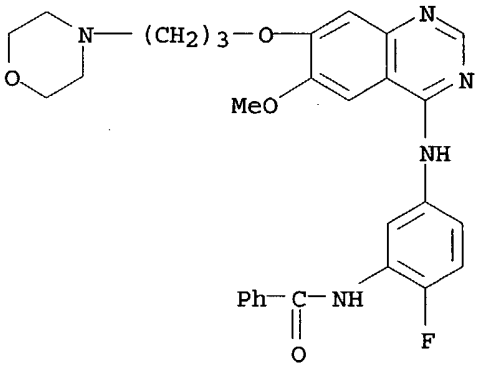
RN 263399-93-5 CAPLUS
CN Benzamide, 4-cyano-N-[3-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-,

monohydrochloride (9CI) (CA INDEX NAME)

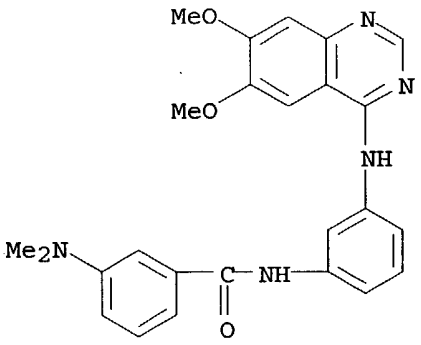


● HCl

RN 263399-94-6 CAPLUS
CN Benzamide, N-[2-fluoro-5-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]- (9CI) (CA INDEX NAME)

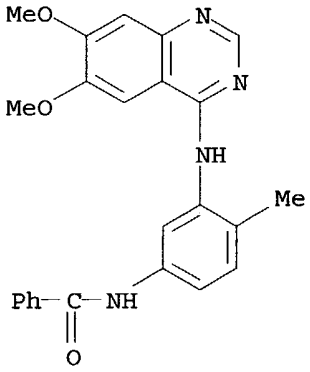


RN 263399-95-7 CAPLUS
CN Benzamide, N-[3-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-3-(dimethylamino)-, monohydrochloride (9CI) (CA INDEX NAME)



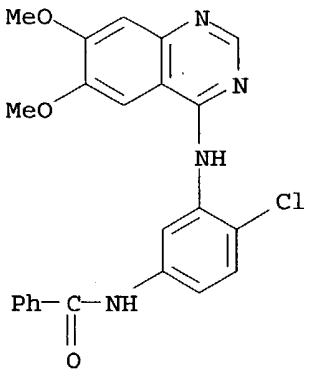
● HCl

RN 263399-96-8 CAPLUS
CN Benzamide, N-[3-[(6,7-dimethoxy-4-quinazolinyl)amino]-4-methylphenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



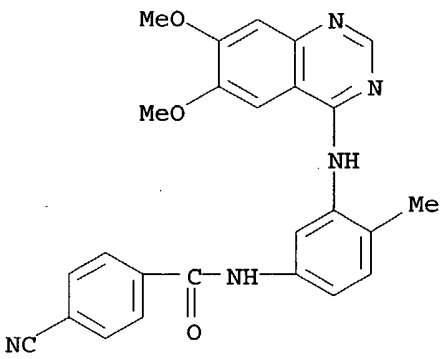
● HCl

RN 263399-97-9 CAPLUS
CN Benzamide, N-[4-chloro-3-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



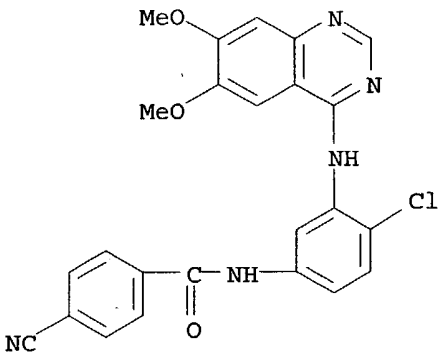
● HCl

RN 263399-98-0 CAPLUS
CN Benzamide, 4-cyano-N-[3-[(6,7-dimethoxy-4-quinazolinyl)amino]-4-methylphenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



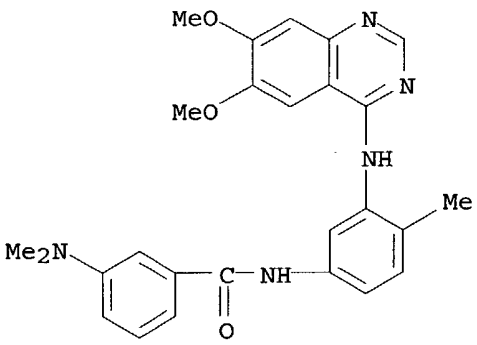
● HCl

RN 263399-99-1 CAPLUS
CN Benzamide, N-[4-chloro-3-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-4-cyano-, monohydrochloride (9CI) (CA INDEX NAME)



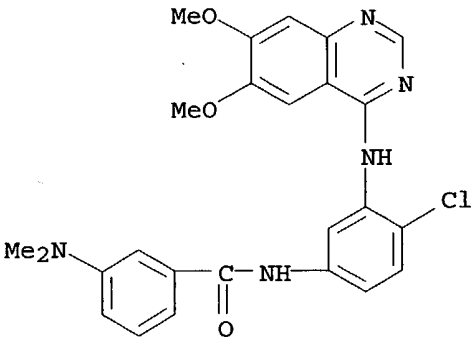
● HCl

RN 263400-00-6 CAPLUS
CN Benzamide, N-[3-[(6,7-dimethoxy-4-quinazolinyl)amino]-4-methylphenyl]-3-(dimethylamino)-, monohydrochloride (9CI) (CA INDEX NAME)



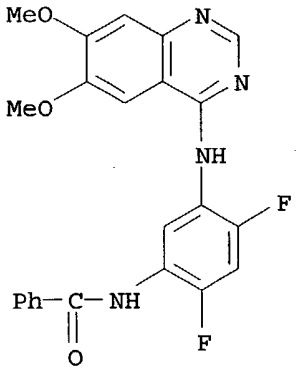
● HCl

RN 263400-01-7 CAPLUS
CN Benzamide, N-[4-chloro-3-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-3-(dimethylamino)-, monohydrochloride (9CI) (CA INDEX NAME)



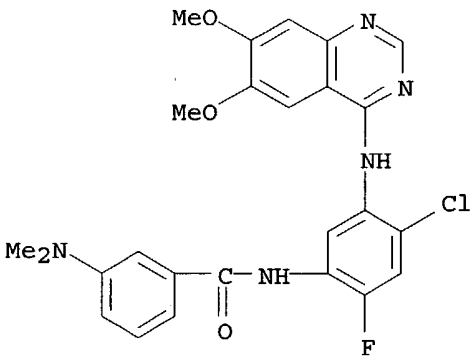
● HCl

RN 263400-03-9 CAPLUS
CN Benzamide, N-[5-[(6,7-dimethoxy-4-quinazolinyl)amino]-2,4-difluorophenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



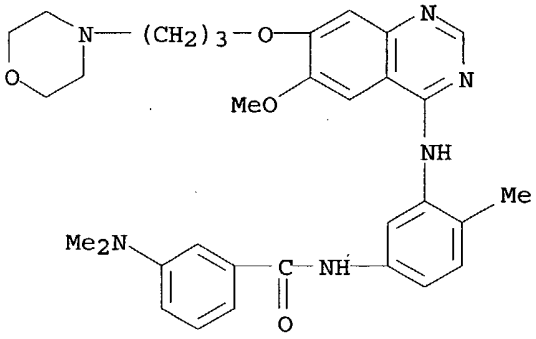
● HCl

RN 263400-04-0 CAPLUS
CN Benzamide, N-[4-chloro-5-[(6,7-dimethoxy-4-quinazolinyl)amino]-2-fluorophenyl]-3-(dimethylamino)-, monohydrochloride (9CI) (CA INDEX NAME)



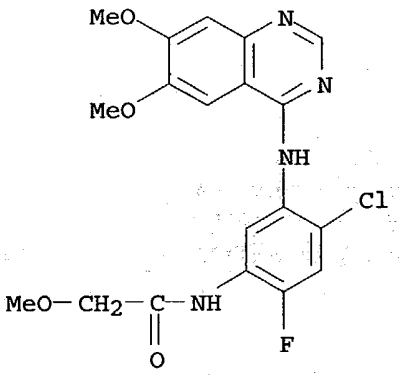
● HCl

RN 263400-05-1 CAPLUS
CN Benzamide, 3-(dimethylamino)-N-[3-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]-4-methylphenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



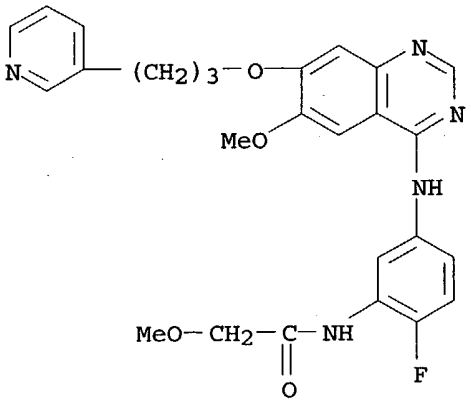
● HCl

RN 263400-06-2 CAPLUS
CN Acetamide, N-[4-chloro-5-[(6,7-dimethoxy-4-quinazolinyl)amino]-2-fluorophenyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)



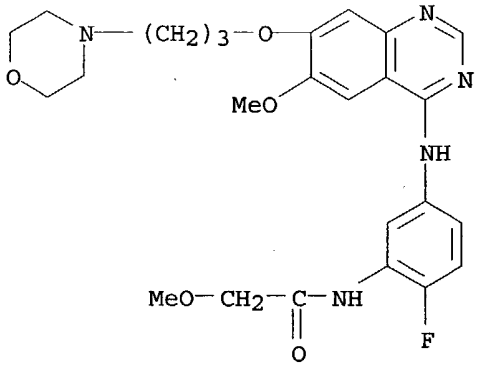
● HCl

RN 263400-07-3 CAPLUS
CN Acetamide, N-[2-fluoro-5-[[6-methoxy-7-[3-(3-pyridinyl)propoxy]-4-quinazolinyl]amino]phenyl]-2-methoxy-, dihydrochloride (9CI) (CA INDEX NAME)



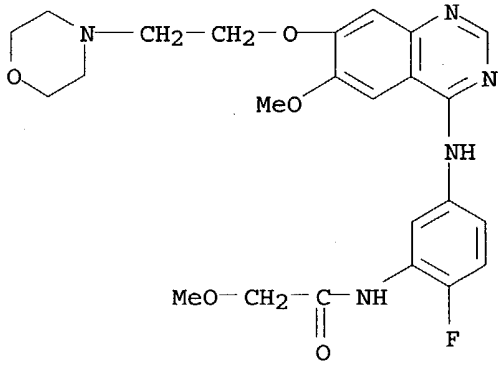
●2 HCl

RN 263400-08-4 CAPLUS
CN Acetamide, N-[2-fluoro-5-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]-2-methoxy-, dihydrochloride (9CI) (CA INDEX NAME)



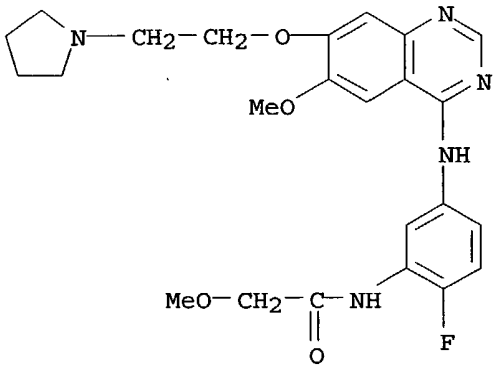
●2 HCl

RN 263400-09-5 CAPLUS
CN Acetamide, N-[2-fluoro-5-[[6-methoxy-7-[2-(4-morpholinyl)ethoxy]-4-quinazolinyl]amino]phenyl]-2-methoxy-, dihydrochloride (9CI) (CA INDEX NAME)



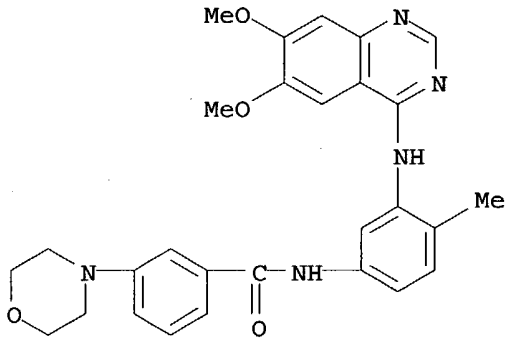
●2 HCl

RN 263400-10-8 CAPLUS
CN Acetamide, N-[2-fluoro-5-[[6-methoxy-7-[2-(1-pyrrolidinyl)ethoxy]-4-quinazolinyl]amino]phenyl]-2-methoxy-, dihydrochloride (9CI) (CA INDEX NAME)



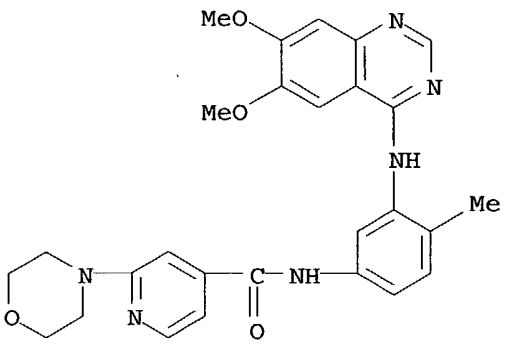
●2 HCl

RN 263400-11-9 CAPLUS
CN Benzamide, N-[3-[(6,7-dimethoxy-4-quinazolinyl)amino]-4-methylphenyl]-3-(4-morpholinyl)-, dihydrochloride (9CI) (CA INDEX NAME)



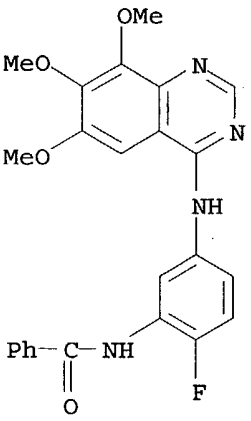
●2 HCl

RN 263400-12-0 CAPLUS
CN 4-Pyridinecarboxamide, N-[3-[(6,7-dimethoxy-4-quinazolinyl)amino]-4-methylphenyl]-2-(4-morpholinyl)-, monohydrochloride (9CI) (CA INDEX NAME)



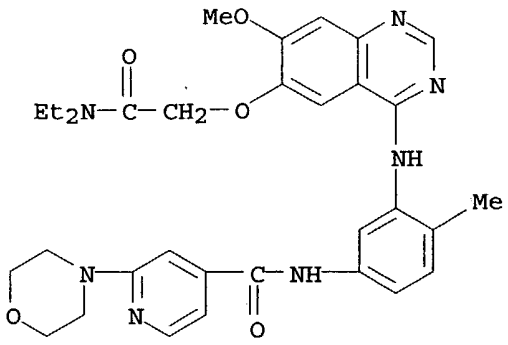
● HCl

RN 263400-13-1 CAPLUS
CN Benzamide, N-[2-fluoro-5-[(6,7,8-trimethoxy-4-quinazolinyl)amino]phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)

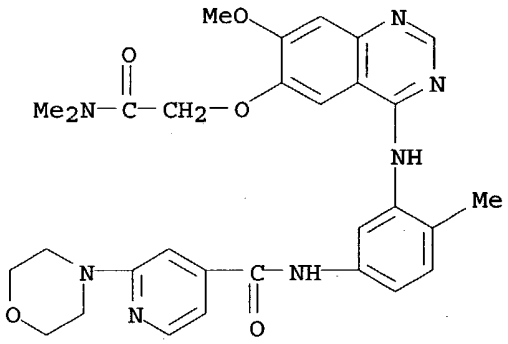


● HCl

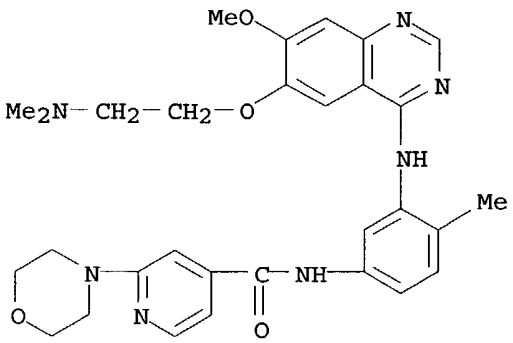
RN 263400-19-7 CAPLUS
CN 4-Pyridinecarboxamide, N-[3-[[6-[2-(diethylamino)-2-oxoethoxy]-7-methoxy-4-quinazolinyl]amino]-4-methylphenyl]-2-(4-morpholinyl)- (9CI) (CA INDEX NAME)



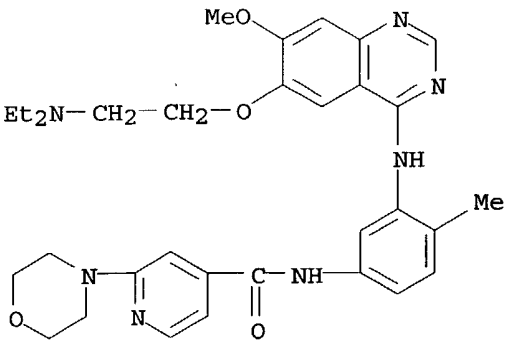
RN 263400-20-0 CAPLUS
CN 4-Pyridinecarboxamide, N-[3-[[6-[2-(dimethylamino)-2-oxoethoxy]-7-methoxy-4-quinazolinyl]amino]-4-methylphenyl]-2-(4-morpholinyl)- (9CI) (CA INDEX NAME)



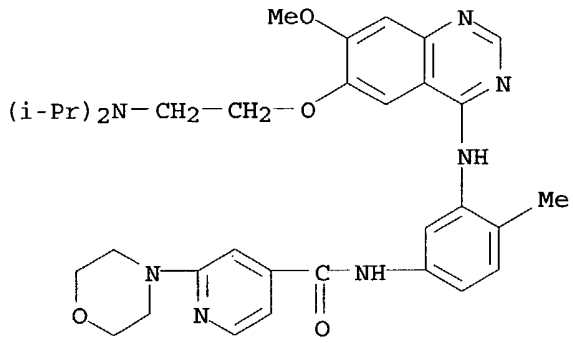
RN 263400-21-1 CAPLUS
CN 4-Pyridinecarboxamide, N-[3-[[6-[2-(dimethylamino)ethoxy]-7-methoxy-4-quinazolinyl]amino]-4-methylphenyl]-2-(4-morpholinyl)- (9CI) (CA INDEX NAME)



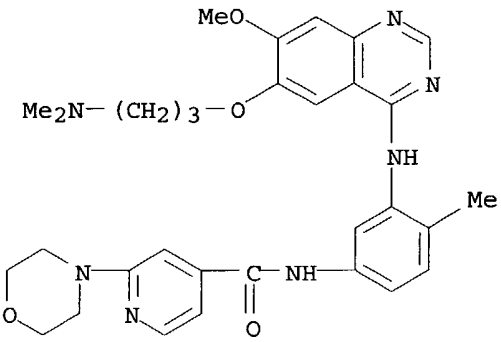
RN 263400-22-2 CAPLUS
CN 4-Pyridinecarboxamide, N-[3-[[6-[2-(diethylamino)ethoxy]-7-methoxy-4-quinazolinyl]amino]-4-methylphenyl]-2-(4-morpholinyl)- (9CI) (CA INDEX NAME)



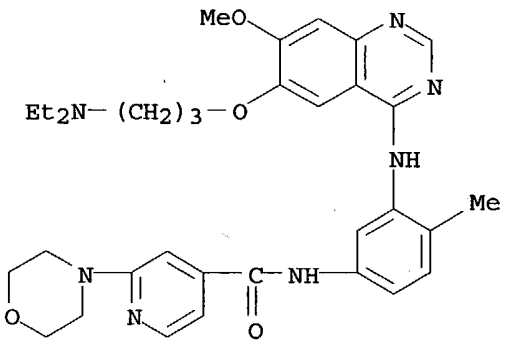
RN 263400-23-3 CAPLUS
CN 4-Pyridinecarboxamide, N-[3-[[6-[2-[bis(1-methylethyl)amino]ethoxy]-7-methoxy-4-quinazolinyl]amino]-4-methylphenyl]-2-(4-morpholinyl)- (9CI) (CA INDEX NAME)



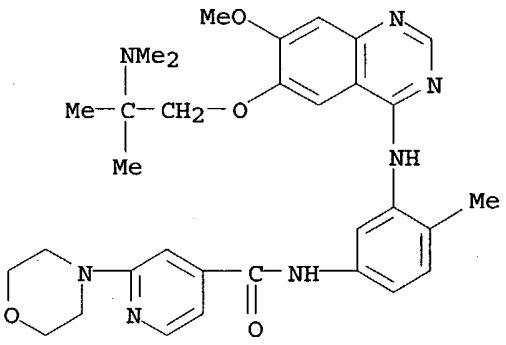
RN 263400-25-5 CAPLUS
CN 4-Pyridinecarboxamide, N-[3-[[6-[3-(dimethylamino)propoxy]-7-methoxy-4-quinazolinyl]amino]-4-methylphenyl]-2-(4-morpholinyl)- (9CI) (CA INDEX NAME)



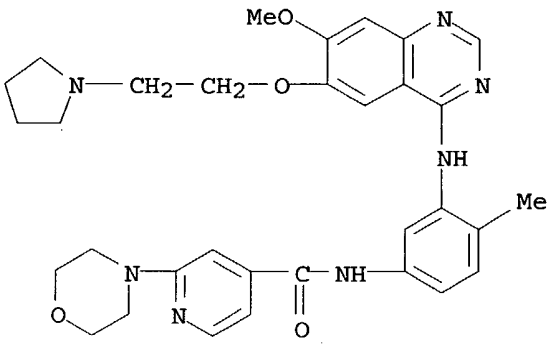
RN 263400-26-6 CAPLUS
CN 4-Pyridinecarboxamide, N-[3-[[6-[3-(diethylamino)propoxy]-7-methoxy-4-quinazolinyl]amino]-4-methylphenyl]-2-(4-morpholinyl)- (9CI) (CA INDEX NAME)



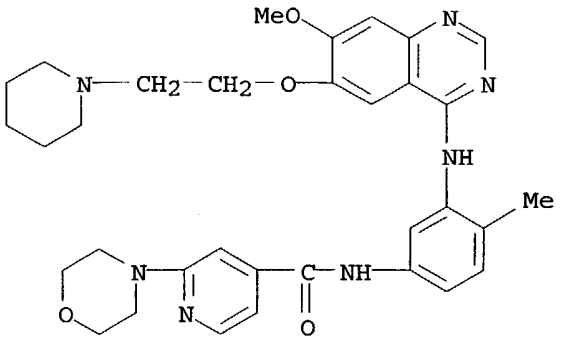
RN 263400-27-7 CAPLUS
CN 4-Pyridinecarboxamide, N-[3-[[6-[2-(dimethylamino)-2-methylpropoxy]-7-methoxy-4-quinazolinyl]amino]-4-methylphenyl]-2-(4-morpholinyl)- (9CI) (CA INDEX NAME)



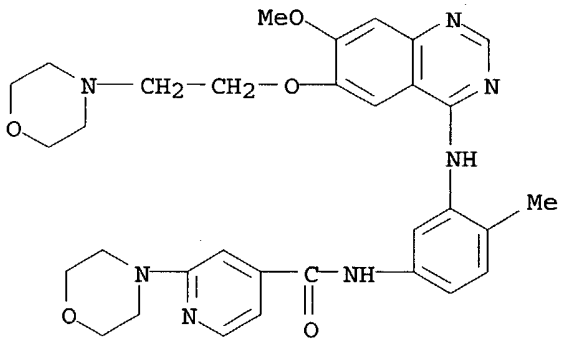
RN 263400-28-8 CAPLUS
CN 4-Pyridinecarboxamide, N-[3-[[7-methoxy-6-[2-(1-pyrrolidinyl)ethoxy]-4-quinazolinyl]amino]-4-methylphenyl]-2-(4-morpholinyl)- (9CI) (CA INDEX NAME)



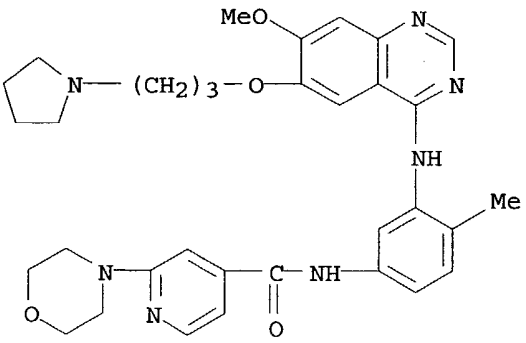
RN 263400-29-9 CAPLUS
CN 4-Pyridinecarboxamide, N-[3-[[7-methoxy-6-[2-(1-piperidinyl)ethoxy]-4-quinazolinyl]amino]-4-methylphenyl]-2-(4-morpholinyl)- (9CI) (CA INDEX NAME)



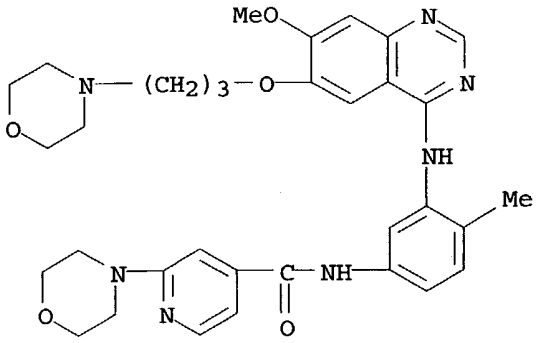
RN 263400-30-2 CAPLUS
CN 4-Pyridinecarboxamide, N-[3-[[7-methoxy-6-[2-(4-morpholinyl)ethoxy]-4-quinazolinyl]amino]-4-methylphenyl]-2-(4-morpholinyl)- (9CI) (CA INDEX NAME)



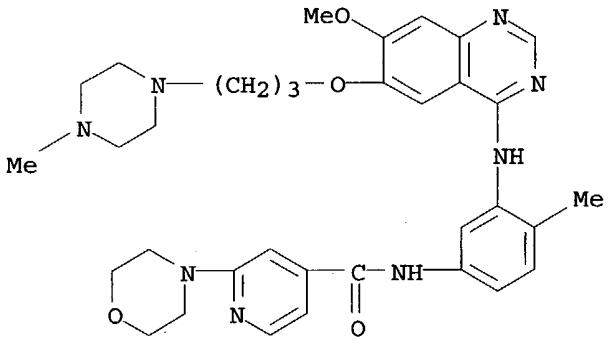
RN 263400-31-3 CAPLUS
CN 4-Pyridinecarboxamide, N-[3-[[7-methoxy-6-[3-(1-pyrrolidinyl)propoxy]-4-quinazolinyl]amino]-4-methylphenyl]-2-(4-morpholinyl)- (9CI) (CA INDEX NAME)



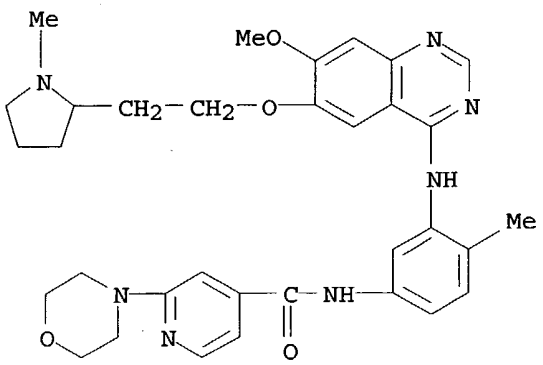
RN 263400-32-4 CAPLUS
CN 4-Pyridinecarboxamide, N-[3-[[7-methoxy-6-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]-4-methylphenyl]-2-(4-morpholinyl)- (9CI) (CA INDEX NAME)



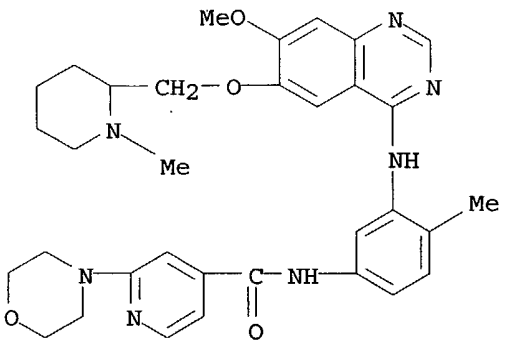
RN 263400-33-5 CAPLUS
CN 4-Pyridinecarboxamide, N-[3-[[7-methoxy-6-[3-(4-methyl-1-piperazinyl)propoxy]-4-quinazolinyl]amino]-4-methylphenyl]-2-(4-morpholinyl)- (9CI) (CA INDEX NAME)



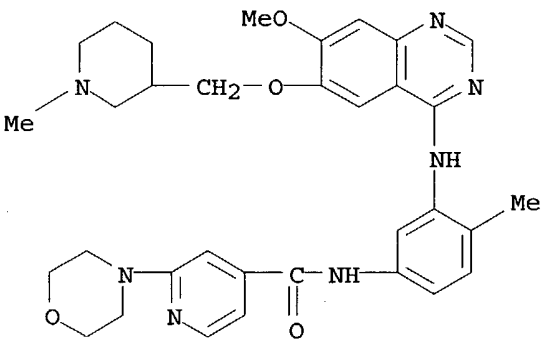
RN 263400-34-6 CAPLUS
CN 4-Pyridinecarboxamide, N-[3-[[7-methoxy-6-[2-(1-methyl-2-pyrrolidinyl)ethoxy]-4-quinazolinyl]amino]-4-methylphenyl]-2-(4-morpholinyl)- (9CI) (CA INDEX NAME)



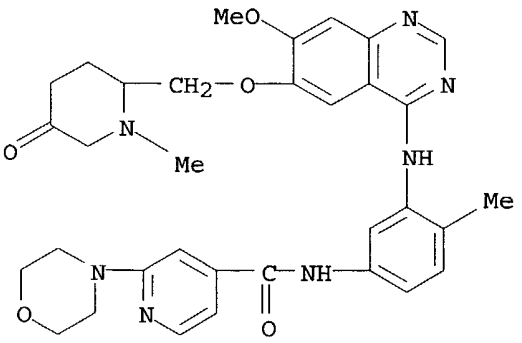
RN 263400-35-7 CAPLUS
CN 4-Pyridinecarboxamide, N-[3-[[7-methoxy-6-[(1-methyl-2-piperidinyl)methoxy]-4-quinazolinyl]amino]-4-methylphenyl]-2-(4-morpholinyl)- (9CI) (CA INDEX NAME)



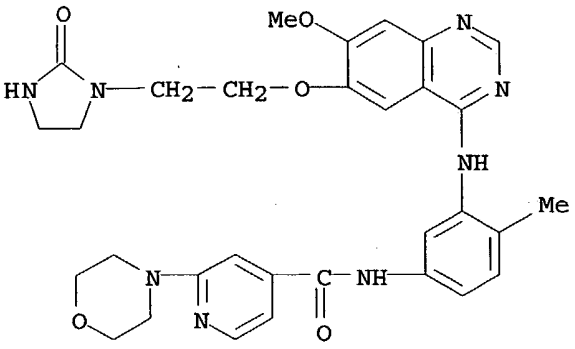
RN 263400-36-8 CAPLUS
CN 4-Pyridinecarboxamide, N-[3-[[7-methoxy-6-[(1-methyl-3-piperidinyl)methoxy]-4-quinazolinyl]amino]-4-methylphenyl]-2-(4-morpholinyl)- (9CI) (CA INDEX NAME)



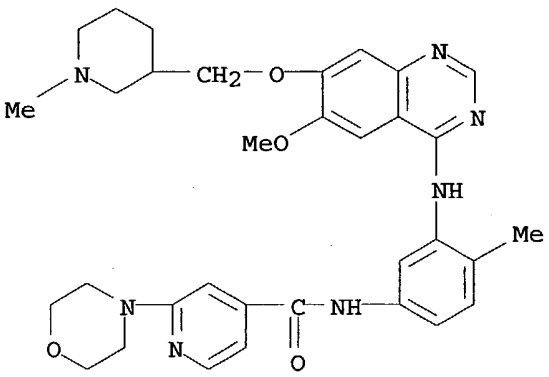
RN 263400-37-9 CAPLUS
CN 4-Pyridinecarboxamide, N-[3-[[7-methoxy-6-[(1-methyl-5-oxo-2-piperidinyl)methoxy]-4-quinazolinyl]amino]-4-methylphenyl]-2-(4-morpholinyl)- (9CI) (CA INDEX NAME)



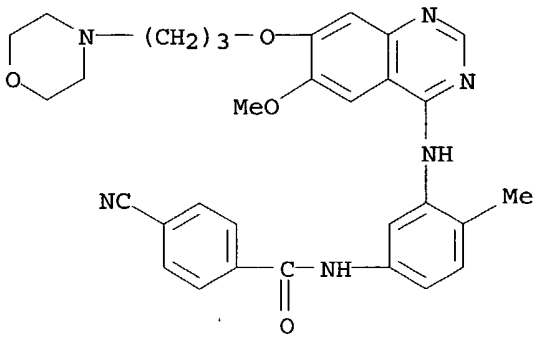
RN 263400-38-0 CAPLUS
CN 4-Pyridinecarboxamide, N-[3-[[7-methoxy-6-[2-(2-oxo-1-imidazolidinyl)ethoxy]-4-quinazolinyl]amino]-4-methylphenyl]-2-(4-morpholinyl)- (9CI) (CA INDEX NAME)



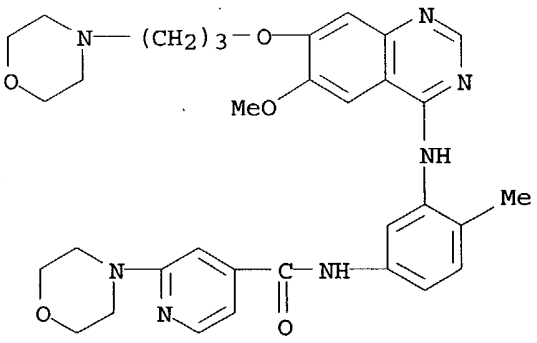
RN 263400-39-1 CAPLUS
CN 4-Pyridinecarboxamide, N-[3-[[6-methoxy-7-[(1-methyl-3-piperidinyl)methoxy]-4-quinazolinyl]amino]-4-methylphenyl]-2-(4-morpholinyl)- (9CI) (CA INDEX NAME)



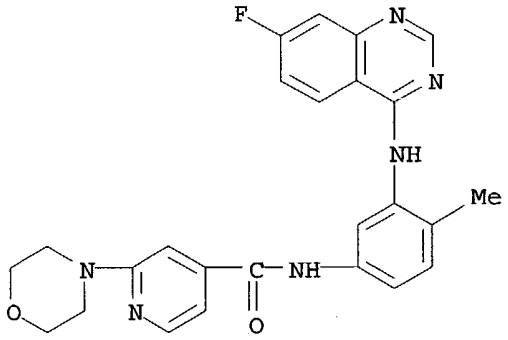
RN 263400-40-4 CAPLUS
CN Benzamide, 4-cyano-N-[3-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]-4-methylphenyl]- (9CI) (CA INDEX NAME)



RN 263400-41-5 CAPLUS
CN 4-Pyridinecarboxamide, N-[3-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]-4-methylphenyl]-2-(4-morpholinyl)- (9CI) (CA INDEX NAME)

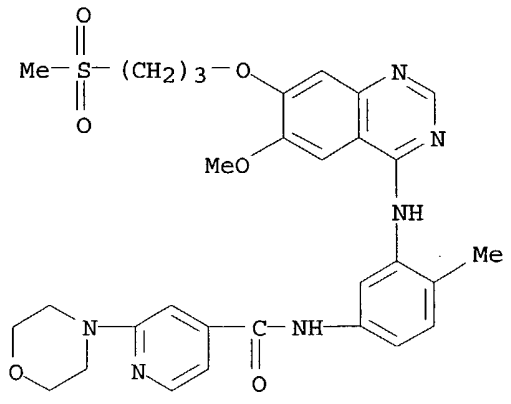


RN 263400-42-6 CAPLUS
CN 4-Pyridinecarboxamide, N-[3-[(7-fluoro-4-quinazolinyl)amino]-4-methylphenyl]-2-(4-morpholinyl)-, dihydrochloride (9CI) (CA INDEX NAME)



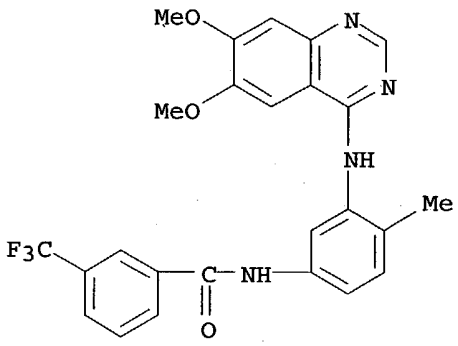
●2 HCl

RN 263400-43-7 CAPLUS
CN 4-Pyridinecarboxamide, N-[3-[[6-methoxy-7-[3-(methylsulfonyl)propoxy]-4-quinazolinyl]amino]-4-methylphenyl]-2-(4-morpholinyl)- (9CI) (CA INDEX NAME)



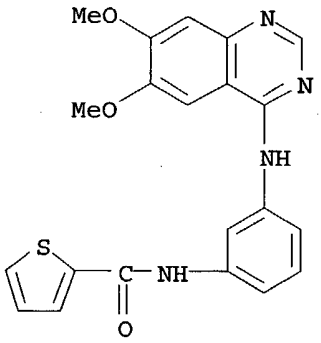
RN 263400-44-8 CAPLUS
CN Benzamide, N-[3-[(6,7-dimethoxy-4-quinazolinyl)amino]-4-methylphenyl]-3-

(trifluoromethyl)-, monohydrochloride (9CI) (CA INDEX NAME)



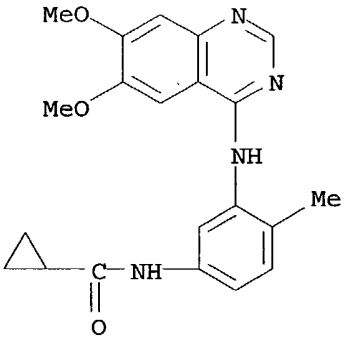
● HCl

RN 263400-45-9 CAPLUS
CN 2-Thiophenecarboxamide, N-[3-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



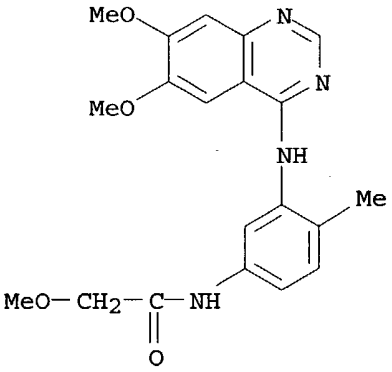
● HCl

RN 263400-46-0 CAPLUS
CN Cyclopropanecarboxamide, N-[3-[(6,7-dimethoxy-4-quinazolinyl)amino]-4-methylphenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



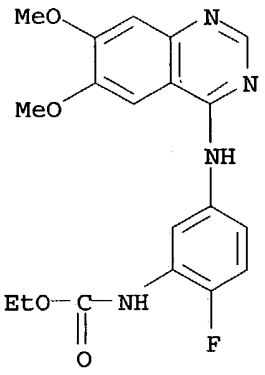
● HCl

RN 263400-48-2 CAPLUS
CN Acetamide, N-[3-[(6,7-dimethoxy-4-quinazolinyl)amino]-4-methylphenyl]-2-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)

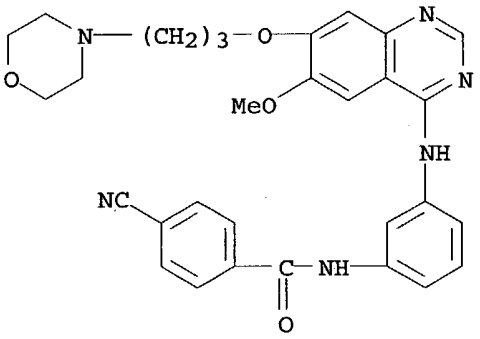


● HCl

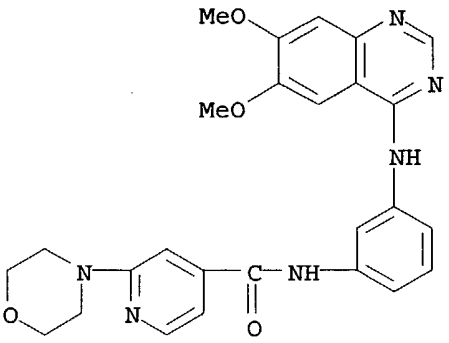
RN 263400-50-6 CAPLUS
CN Carbamic acid, [5-[(6,7-dimethoxy-4-quinazolinyl)amino]-2-fluorophenyl]-, ethyl ester (9CI) (CA INDEX NAME)



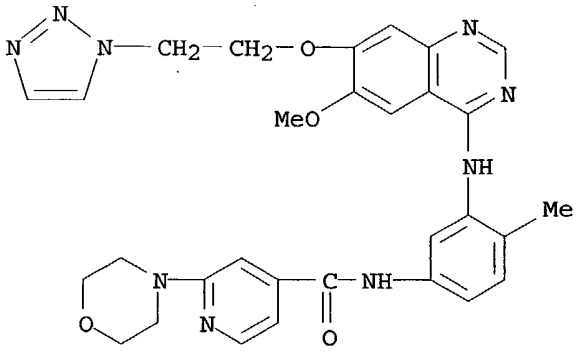
RN 263400-51-7 CAPLUS
CN Benzamide, 4-cyano-N-[3-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



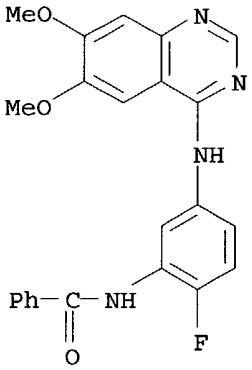
RN 263400-52-8 CAPLUS
CN 4-Pyridinecarboxamide, N-[3-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-2-(4-morpholinyl)- (9CI) (CA INDEX NAME)



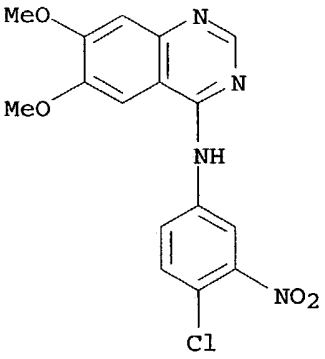
RN 263400-53-9 CAPLUS
CN 4-Pyridinecarboxamide, N-[3-[[6-methoxy-7-[2-(1H-1,2,3-triazol-1-yl)ethoxy]-4-quinazolinyl]amino]-4-methylphenyl]-2-(4-morpholinyl)- (9CI) (CA INDEX NAME)



RN 263400-94-8 CAPLUS
CN Benzamide, N-[5-[(6,7-dimethoxy-4-quinazolinyl)amino]-2-fluorophenyl]-
(9CI) (CA INDEX NAME)

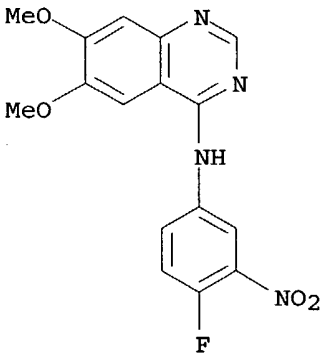


IT **153437-08-2P 153437-09-3P 263400-54-0P**
263400-55-1P 263400-56-2P 263400-57-3P
263400-58-4P 263400-59-5P 263400-60-8P
263400-61-9P 263400-62-0P 263400-63-1P
263400-64-2P 263400-86-8P 263400-87-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(prepn. of 4-anilinoquinazolines and 4-anilinoquinolines as inhibitors
of cytokine mediated disease)
RN 153437-08-2 CAPLUS
CN 4-Quinazolinamine, N-(4-chloro-3-nitrophenyl)-6,7-dimethoxy-,
monohydrochloride (9CI) (CA INDEX NAME)



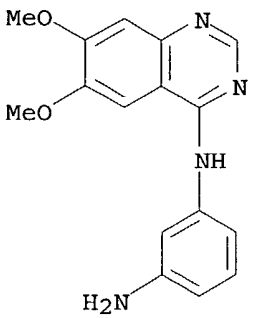
● HCl

RN 153437-09-3 CAPLUS
CN 4-Quinazolinamine, N-(4-fluoro-3-nitrophenyl)-6,7-dimethoxy-, monohydrochloride (9CI) (CA INDEX NAME)

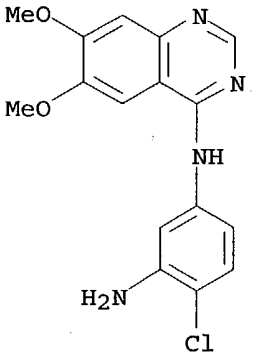


● HCl

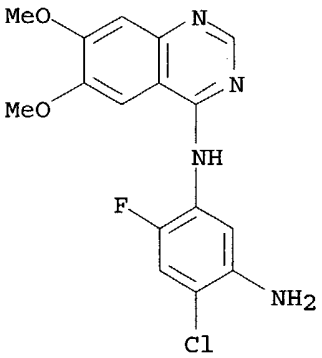
RN 263400-54-0 CAPLUS
CN 1,3-Benzenediamine, N-(6,7-dimethoxy-4-quinazolinyl)- (9CI) (CA INDEX NAME)



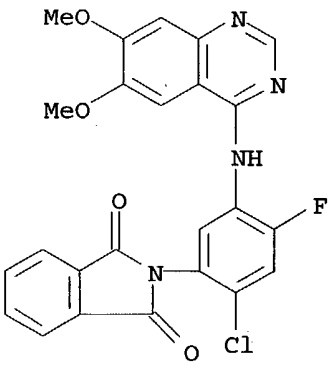
RN 263400-55-1 CAPLUS
CN 1,3-Benzenediamine, 4-chloro-N1-(6,7-dimethoxy-4-quinazolinyl)- (9CI) (CA INDEX NAME)



RN 263400-56-2 CAPLUS
CN 1,3-Benzenediamine, 4-chloro-N1-(6,7-dimethoxy-4-quinazolinyl)-6-fluoro- (9CI) (CA INDEX NAME)

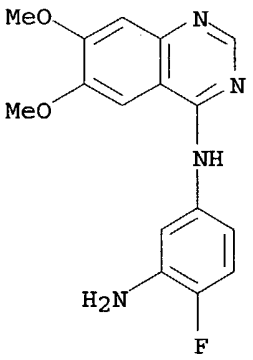


RN 263400-57-3 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-chloro-5-[(6,7-dimethoxy-4-quinazolinyl)amino]-4-fluorophenyl]-, monohydrochloride (9CI) (CA INDEX NAME)

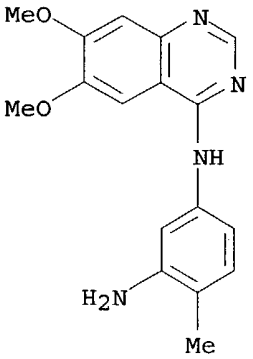


● HCl

RN 263400-58-4 CAPLUS
CN 1,3-Benzenediamine, N1-(6,7-dimethoxy-4-quinazolinyl)-4-fluoro- (9CI) (CA INDEX NAME)

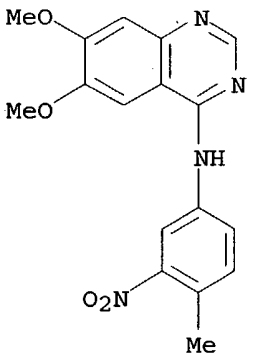


RN 263400-59-5 CAPLUS
CN 1,3-Benzenediamine, N1-(6,7-dimethoxy-4-quinazolinyl)-4-methyl- (9CI) (CA INDEX NAME)



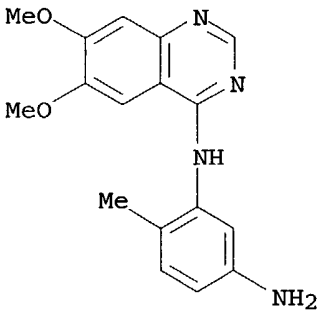
RN 263400-60-8 CAPLUS
CN 4-Quinazolinamine, 6,7-dimethoxy-N-(4-methyl-3-nitrophenyl)-,

monohydrochloride (9CI) (CA INDEX NAME)

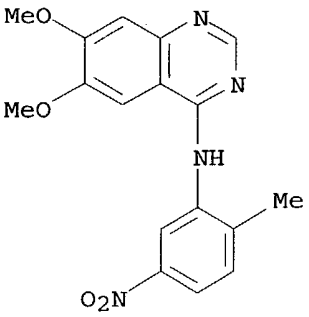


● HCl

RN 263400-61-9 CAPLUS
CN 1,3-Benzenediamine, N3-(6,7-dimethoxy-4-quinazolinyl)-4-methyl- (9CI) (CA INDEX NAME)

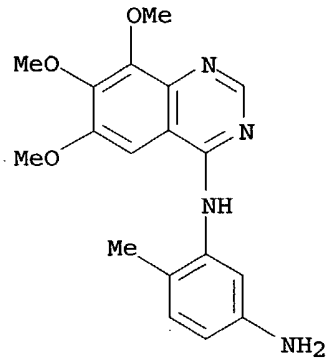


RN 263400-62-0 CAPLUS
CN 4-Quinazolinamine, 6,7-dimethoxy-N-(2-methyl-5-nitrophenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

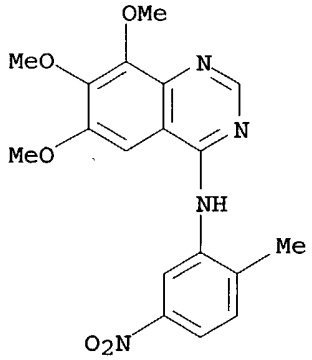


● HCl

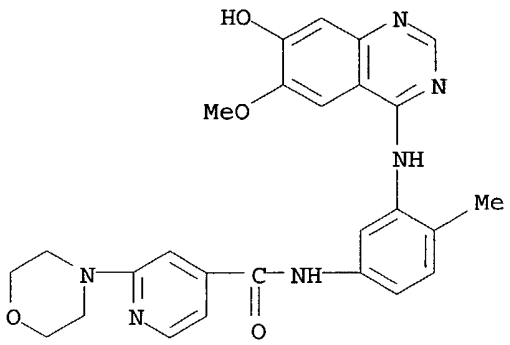
RN 263400-63-1 CAPLUS
CN 1,3-Benzenediamine, 4-methyl-N3-(6,7,8-trimethoxy-4-quinazolinyl)- (9CI) (CA INDEX NAME)



RN 263400-64-2 CAPLUS
CN 4-Quinazolinamine, 6,7,8-trimethoxy-N-(2-methyl-5-nitrophenyl)- (9CI) (CA INDEX NAME)

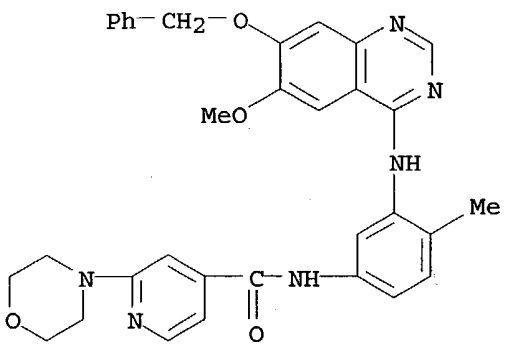


RN 263400-86-8 CAPLUS
CN 4-Pyridinecarboxamide, N-[3-[(7-hydroxy-6-methoxy-4-quinazolinyl)amino]-4-methylphenyl]-2-(4-morpholinyl)- (9CI) (CA INDEX NAME)



RN 263400-87-9 CAPLUS
CN 4-Pyridinecarboxamide, N-[3-[[6-methoxy-7-(phenylmethoxy)-4-

quinazolinyl]amino]-4-methylphenyl]-2-(4-morpholinyl)-, dihydrochloride (9CI) (CA INDEX NAME)



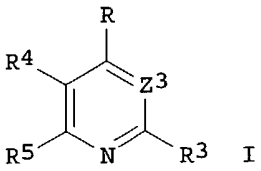
●2 HCl

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 14 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:161275 CAPLUS
DOCUMENT NUMBER: 132:194387
TITLE: Preparation of quinazolines as **p38**-. **alpha**. **kinase** and TGF-.beta. inhibitors
INVENTOR(S): Chakravarty, Sarvajit; Dugar, Sundeep; Perumattam, John J.; Schreiner, George F.; Liu, David Y.; Lewicki, John A.
PATENT ASSIGNEE(S): Scios Inc., USA
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000012497	A2	20000309	WO 1999-US19846	19990827
WO 2000012497	A3	20000629		
W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CR, CU, CZ, EE, GE, HU, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6184226	B1	20010206	US 1998-141916	19980828
CA 2342250	AA	20000309	CA 1999-2342250	19990827
AU 9962413	A1	20000321	AU 1999-62413	19990827
AU 771947	B2	20040408		
EP 1107959	A2	20010620	EP 1999-949568	19990827
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9913648	A	20020102	BR 1999-13648	19990827

JP 2002523502 T2 20020730 JP 2000-567525 19990827
PRIORITY APPLN. INFO.: US 1998-141916 A 19980828
WO 1999-US19846 W 19990827
OTHER SOURCE(S): MARPAT 132:194387
ED Entered STN: 10 Mar 2000
GI



I

AB Title compds. [I; R = ZR1; R1 = (un)substituted cyclic (hetero)aliph. group, -(hetero)aryl; R3 = noninterfering substituent (sic); R4R5 = atoms to complete a 6-membered arom. ring contg. 0, 1, or 2 nonadjacent N atoms and noninterfering substituent(s) (sic); z = bond or linker (sic); Z3 = CR2 or N; R2 = noninterfering substituent (sic)] were prepd. Thus, prepn of, e.g., 4-(4-pyridinylamino)-2-phenylquinazoline was described. Data for biol. activity of I were given.

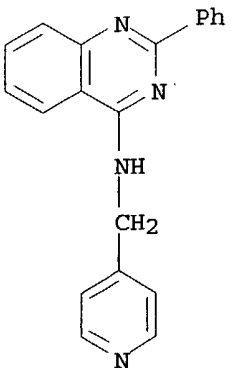
IT **165245-96-5**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(mediated disorders; treatment; prepn. of quinazolines as **p38 -.alpha. kinase** and TGF-.beta. inhibitors)

RN 165245-96-5 CAPLUS
CN Kinase (phosphorylating), protein, RK (9CI) (CA INDEX NAME)

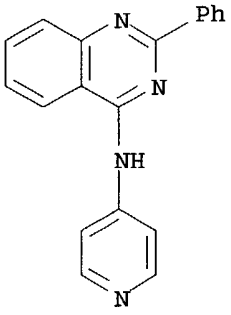
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **259870-32-1P 259870-33-2P 259870-34-3P**
259870-35-4P 259870-36-5P 259870-37-6P
259870-38-7P 259870-39-8P 259870-40-1P
259870-41-2P 259870-42-3P 259870-43-4P
259870-44-5P 259870-45-6P 259870-46-7P
259870-47-8P 259870-48-9P 259870-49-0P
259870-50-3P 259870-51-4P 259870-52-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of quinazolines as **p38-.alpha. kinase** and TGF-.beta. inhibitors)

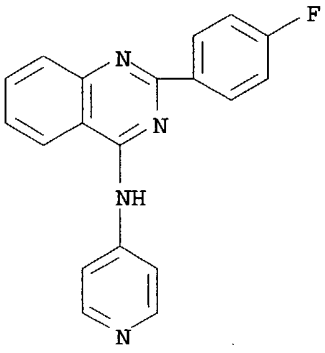
RN 259870-32-1 CAPLUS
CN 4-Quinazolinamine, 2-phenyl-N-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



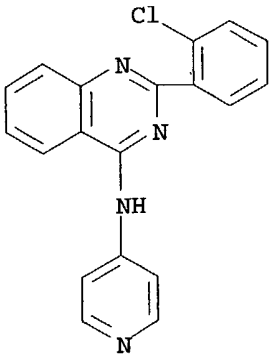
RN 259870-33-2 CAPLUS
CN 4-Quinazolinamine, 2-phenyl-N-4-pyridinyl- (9CI) (CA INDEX NAME)



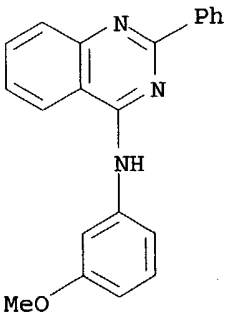
RN 259870-34-3 CAPLUS
CN 4-Quinazolinamine, 2-(4-fluorophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



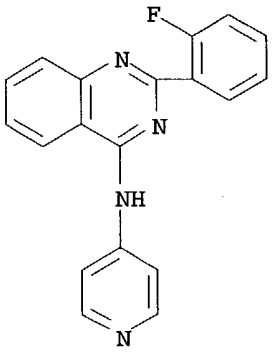
RN 259870-35-4 CAPLUS
CN 4-Quinazolinamine, 2-(2-chlorophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



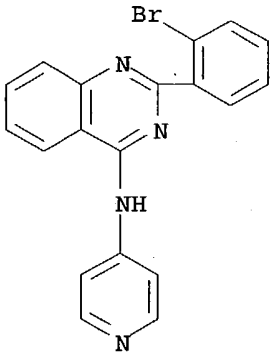
RN 259870-36-5 CAPLUS
CN 4-Quinazolinamine, N-(3-methoxyphenyl)-2-phenyl- (9CI) (CA INDEX NAME)



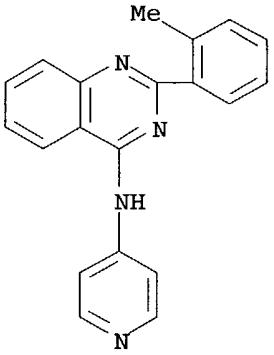
RN 259870-37-6 CAPLUS
CN 4-Quinazolinamine, 2-(2-fluorophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



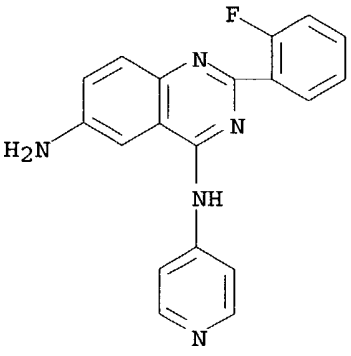
RN 259870-38-7 CAPLUS
CN 4-Quinazolinamine, 2-(2-bromophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



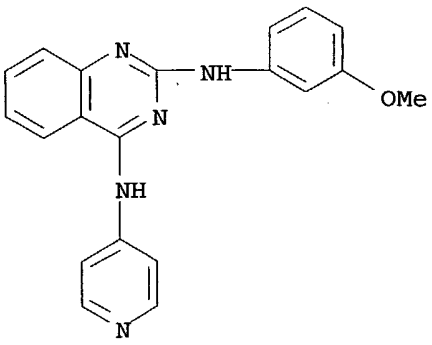
RN 259870-39-8 CAPLUS
CN 4-Quinazolinamine, 2-(2-methylphenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



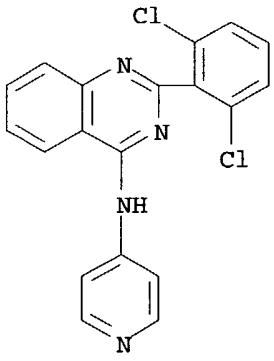
RN 259870-40-1 CAPLUS
CN 4,6-Quinazolinediamine, 2-(2-fluorophenyl)-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



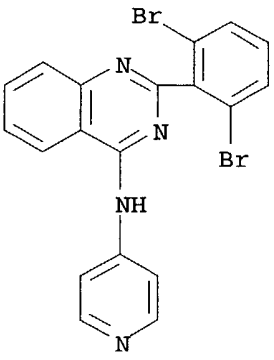
RN 259870-41-2 CAPLUS
CN 2,4-Quinazolinediamine, N2-(3-methoxyphenyl)-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



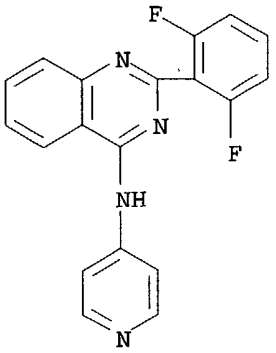
RN 259870-42-3 CAPLUS
CN 4-Quinazolinamine, 2-(2,6-dichlorophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



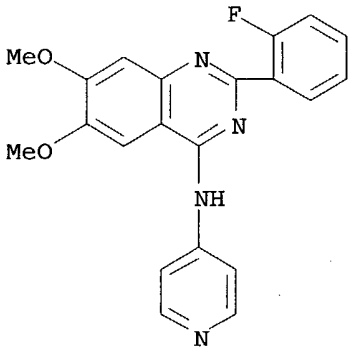
RN 259870-43-4 CAPLUS
CN 4-Quinazolinamine, 2-(2,6-dibromophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



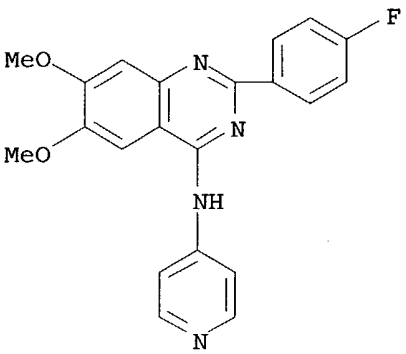
RN 259870-44-5 CAPLUS
CN 4-Quinazolinamine, 2-(2,6-difluorophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



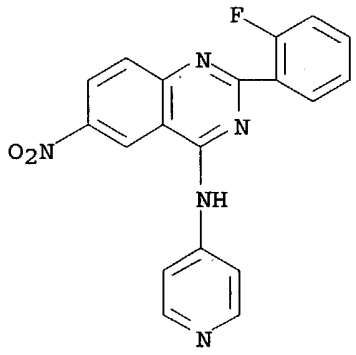
RN 259870-45-6 CAPLUS
CN 4-Quinazolinamine, 2-(2-fluorophenyl)-6,7-dimethoxy-N-4-pyridinyl- (9CI) (CA INDEX NAME)



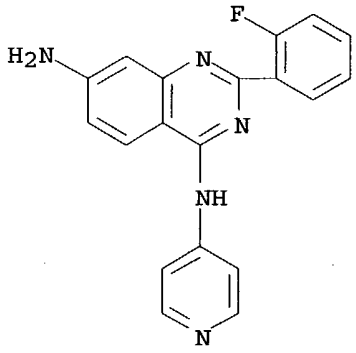
RN 259870-46-7 CAPLUS
CN 4-Quinazolinamine, 2-(4-fluorophenyl)-6,7-dimethoxy-N-4-pyridinyl- (9CI) (CA INDEX NAME)



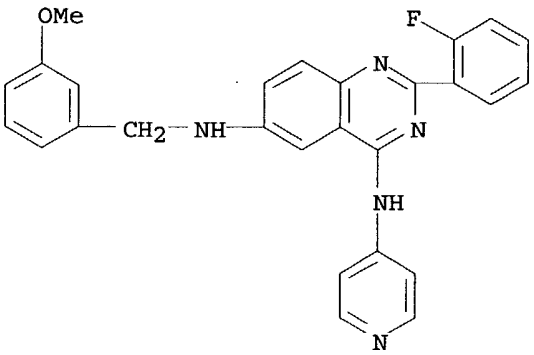
RN 259870-47-8 CAPLUS
CN 4-Quinazolinamine, 2-(2-fluorophenyl)-6-nitro-N-4-pyridinyl- (9CI) (CA INDEX NAME)



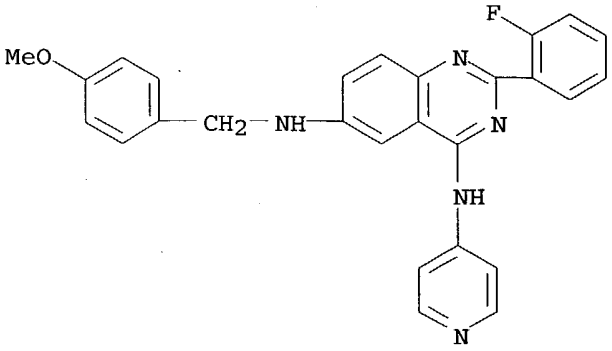
RN 259870-48-9 CAPLUS
CN 4,7-Quinazolinediamine, 2-(2-fluorophenyl)-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



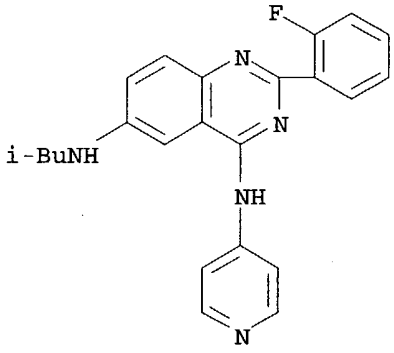
RN 259870-49-0 CAPLUS
CN 4,6-Quinazolinediamine, 2-(2-fluorophenyl)-N6-[(3-methoxyphenyl)methyl]-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



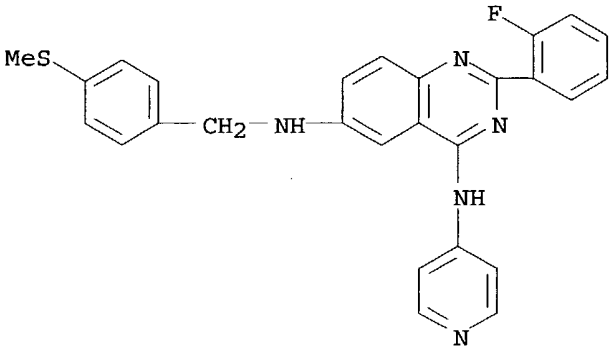
RN 259870-50-3 CAPLUS
CN 4,6-Quinazolinediamine, 2-(2-fluorophenyl)-N6-[(4-methoxyphenyl)methyl]-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



RN 259870-51-4 CAPLUS
CN 4,6-Quinazolinediamine, 2-(2-fluorophenyl)-N6-(2-methylpropyl)-N4-4-pyridinyl- (9CI) (CA INDEX NAME)

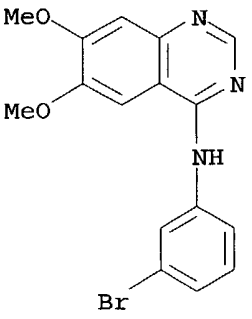


RN 259870-52-5 CAPLUS
CN 4,6-Quinazolinediamine, 2-(2-fluorophenyl)-N6-[[4-(methylthio)phenyl]methyl]-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



L41 ANSWER 15 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:718482 CAPLUS
DOCUMENT NUMBER: 134:50976
TITLE: Classification of Kinase Inhibitors Using BCUT Descriptors

AUTHOR(S): Pirard, Bernard; Pickett, Stephen D.
CORPORATE SOURCE: Aventis Pharma, Dagenham Research Centre, Dagenham Essex, RM10 7XS, UK
SOURCE: Journal of Chemical Information and Computer Sciences (2000), 40(6), 1431-1440
CODEN: JCISD8; ISSN: 0095-2338
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 12 Oct 2000
AB BCUTs are an interesting class of mol. descriptor which have been proposed for a no. of design and QSAR type tasks. It is important to understand what kind of information any particular descriptor encodes and to be able to relate this to the biol. properties of the mols. In this paper the authors present studies with BCUTs for the classification of ATP site directed kinase inhibitors active against five different protein kinases: three from the serine/threonine family and two from the tyrosine kinase family. In combination with a chemometric method, PLS discriminant anal., the BCUTs are able to correctly classify the ligands according to their target. A novel class of kinase inhibitors is correctly predicted as inhibitors of the EGFR tyrosine kinase. Comparison with other descriptor types such as two-dimensional fingerprints and three-dimensional pharmacophore-based descriptors allows the authors to gain an insight into the level of information contained within the BCUTs.
IT **153436-54-5**, PD153035 **171179-29-6 256521-38-7**
313345-15-2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(classification of protein kinase inhibitors directed towards ATP site using BCUT descriptors)
RN 153436-54-5 CAPLUS
CN 4-Quinazolinamine, N-(3-bromophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



RN 171179-29-6 CAPLUS
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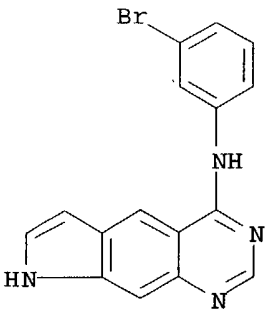
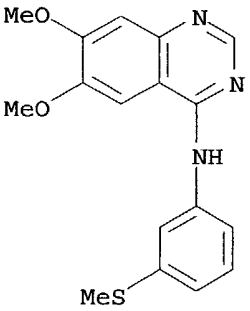
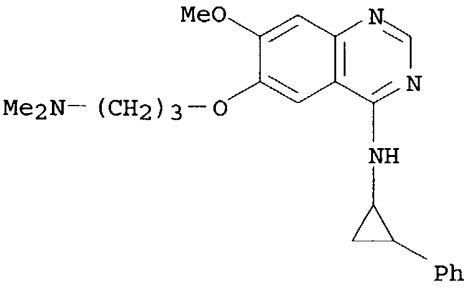


RN 256521-38-7 CAPLUS
CN 4-Quinazolinamine, 6,7-dimethoxy-N-[3-(methylthio)phenyl]- (9CI) (CA INDEX NAME)



RN 313345-15-2 CAPLUS
CN 4-Quinazolinamine, 6-[3-(dimethylamino)propoxy]-7-methoxy-N-(2-phenylcyclopropyl)- (9CI) (CA INDEX NAME)

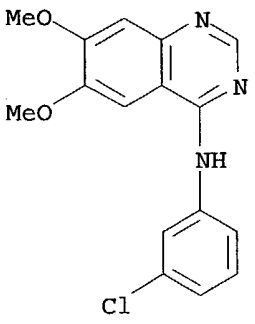


IT **165245-96-5, p38 Kinase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(classification of protein kinase inhibitors directed towards ATP site using BCUT descriptors)
RN 165245-96-5 CAPLUS
CN Kinase (phosphorylating), protein, RK (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
REFERENCE COUNT: 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 16 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN

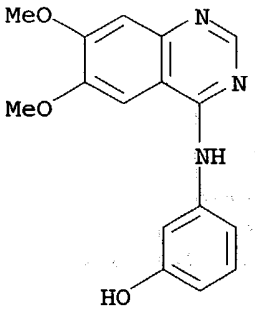
ACCESSION NUMBER: 2000:259048 CAPLUS
DOCUMENT NUMBER: 133:27497
TITLE: Peroxynitrite Modulates the Activation of p38 and Extracellular Regulated Kinases in PC12 Cells
AUTHOR(S): Jope, Richard S.; Zhang, Liang; Song, Ling
CORPORATE SOURCE: Department of Psychiatry and Behavioral Neurobiology, University of Alabama at Birmingham, Birmingham, AL, 35294-0017, USA
SOURCE: Archives of Biochemistry and Biophysics (2000), 376(2), 365-370
CODEN: ABBIA4; ISSN: 0003-9861
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 21 Apr 2000
AB Although peroxynitrite appears to contribute to neuronal dysfunction in several neurodegenerative disorders, little is known about how peroxynitrite affects cellular signaling processes. This study investigated if peroxynitrite affects the mitogen-activated protein kinases, extracellular-regulated kinases 1 and 2 (ERK1/2) and p38. Exposure of PC12 cells to 500 .mu.M peroxynitrite activated ERK1/2 and p38 within 5 min and this was followed by gradual decreases in activation over the next 25 min. Activation of ERK1/2 by peroxynitrite was mediated by activation of the epidermal growth factor (EGF) receptor in a calcium/calmodulin-dependent kinase II- and src family tyrosine kinase-dependent manner, as it was blocked by the selective EGF receptor inhibitor AG1478, by KN62, an inhibitor of calcium/calmodulin-dependent kinase II, and by PP1, a src family tyrosine kinase inhibitor. Activation of p38 by peroxynitrite was independent of the EGF receptor, required activation of calcium/calmodulin-dependent kinase II and src family tyrosine kinases, and was modulated by nerve growth factor (NGF) in a time-dependent manner. Pretreatment with NGF (2 h) attenuated, whereas cotreatment with NGF potentiated, peroxynitrite-induced activation of p38. Thus, peroxynitrite activates ERK1/2 and p38, activation of EGF receptors, calcium/calmodulin-dependent kinase II, and src family tyrosine kinases participate in these signaling responses to peroxynitrite, and peroxynitrite- and NGF-induced signaling activities converge on p38. (c) 2000 Academic Press.
IT **153436-53-4**, AG1478
RL: ARG (Analytical reagent use); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(EGF receptor inhibitor; peroxynitrite modulates the activation of p38 and extracellular regulated kinases in PC12 cells)
RN 153436-53-4 CAPLUS
CN 4-Quinazolinamine, N-(3-chlorophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)



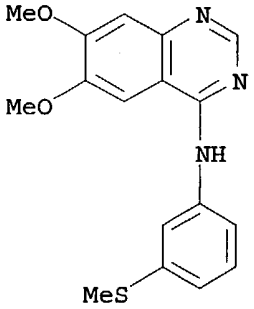
IT **165245-96-5, p38** MAP **kinase**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(peroxynitrite modulates the activation of p38 and extracellular regulated kinases in PC12 cells)
RN 165245-96-5 CAPLUS
CN Kinase (phosphorylating), protein, RK (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 17 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:777762 CAPLUS
DOCUMENT NUMBER: 132:132307
TITLE: Binding mode of the 4-anilinoquinazoline class of protein kinase inhibitor: X-ray crystallographic studies of 4-anilinoquinazolines bound to cyclin-dependent **kinase** 2 and **p38 kinase**
AUTHOR(S): Shewchuk, Lisa; Hassell, Anne; Wisely, Bruce; Rocque, Warren; Holmes, William; Veal, James; Kuyper, Lee F.
CORPORATE SOURCE: Glaxo Wellcome Inc., Research Triangle Park, NC, 27709, USA
SOURCE: Journal of Medicinal Chemistry (2000), 43(1), 133-138
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 09 Dec 1999
AB 4-Anilinoquinazolines represent an important class of protein kinase inhibitor. Modes of binding for two members of this inhibitor class were detd. by x-ray crystallog. anal. of one inhibitor (4-[3-hydroxyanilino]-6,7-dimethoxyquinazoline) in complex with cyclin-dependent kinase 2 (CDK2) and the other (4-[3-methylsulfanylanilino]-6,7-dimethoxyquinazoline) in complex with p38 kinase. In both inhibitor/kinase structures, the 4-anilinoquinazoline was bound in the ATP site with the quinazoline ring system oriented along the peptide strand that links the two domains of the protein and with the anilino substituent projecting into a hydrophobic pocket within the protein interior. In each case, the nitrogen at position-1 of the quinazoline accepted a hydrogen bond from a backbone NH (CDK2, Leu-83; p38, Met-109) of the domain connector strand, and arom. hydrogen atoms at C2 and C8 interacted with backbone carbonyl oxygen atoms of the peptide strand. The anilino group of the CDK2-bound compd. was essentially coplanar with the quinazoline ring system and occupied a pocket between Lys-33 and Phe-80. For the p38-bound inhibitor, the anilino group was angled out of plane and was positioned between Lys-53 and Thr-106 in a manner similar to that obsd. for the aryl substituent of the pyridinylimidazole class of inhibitor.
IT **211555-08-7 256521-38-7**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(x-ray crystallog. of 4-anilinoquinazoline class of protein kinase inhibitor binding to cyclin-dependent **kinase** 2 and **p38 kinase**)
RN 211555-08-7 CAPLUS
CN Phenol, 3-[(6,7-dimethoxy-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



RN 256521-38-7 CAPLUS
CN 4-Quinazolinamine, 6,7-dimethoxy-N-[3-(methylthio)phenyl]- (9CI) (CA INDEX NAME)



IT **165245-96-5D, p38 Kinase**, complexes with 4-anilinoquinazolines
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(x-ray crystallog. of 4-anilinoquinazoline class of protein kinase inhibitor binding to cyclin-dependent **kinase** 2 and **p38 kinase**)
RN 165245-96-5 CAPLUS
CN Kinase (phosphorylating), protein, RK (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 18 OF 37 USPATFULL on STN
ACCESSION NUMBER: 2004:114693 USPATFULL
TITLE: Method of treating conditions related to platelet activity
INVENTOR(S): Du, Xiaoping, Westmont, IL, UNITED STATES

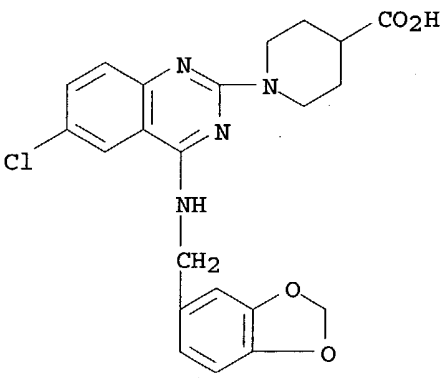
	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2004087539	A1	20040506	
APPLICATION INFO.:	US 2003-467387	A1	20031212	(10)
	WO 2002-US3372		20020205	

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MARSHALL, GERSTEIN & BORUN LLP, 6300 SEARS TOWER, 233 S. WACKER DRIVE, CHICAGO, IL, 60606
NUMBER OF CLAIMS: 14

EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 8 Drawing Page(s)
LINE COUNT: 1427
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods of treating thrombotic and hemostatic conditions related to platelet activity are described herein. The methods of treating thrombotic and hemostatic conditions use active agents that modulate production of guanosine 3', 5' cyclic monophosphate (cGMP) or the function of cGMP-dependent protein kinase (PKG), and its downstream effectors, the ERK and p38 pathways.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **165245-96-5, p38 Kinase**
(cyclic GMP- and protein kinase G-based method of treating conditions related to platelet activity)
RN 165245-96-5 USPATFULL
CN Kinase (phosphorylating), protein, RK (9CI) (CA INDEX NAME)

STRUCTURE DIAGRAM IS NOT AVAILABLE
IT **150452-19-0**, E4021
(cyclic GMP- and protein kinase G-based method of treating conditions related to platelet activity)
RN 150452-19-0 USPATFULL
CN 4-Piperidinecarboxylic acid, 1-[4-[(1,3-benzodioxol-5-ylmethyl)amino]-6-chloro-2-quinazolinyl]-, monosodium salt (9CI) (CA INDEX NAME)



● Na

L41 ANSWER 19 OF 37 USPATFULL on STN
ACCESSION NUMBER: 2004:51425 USPATFULL
TITLE: Treatment of fibroproliferative disorders using TGF-beta inhibitors
INVENTOR(S): Chakravarty, Sarvajit, Sunnyvale, CA, UNITED STATES
Dugar, Sundeep, San Jose, CA, UNITED STATES
Higgins, Linda S., Palo Alto, CA, UNITED STATES
Kapoun, Ann M., Palo Alto, CA, UNITED STATES
Liu, David Y., Palo Alto, CA, UNITED STATES
Protter, Andrew A., Palo Alto, CA, UNITED STATES
Schreiner, George F., Los Altos, CA, UNITED STATES
Tran, Thomas-Toan, Sunnyvale, CA, UNITED STATES

NUMBER KIND DATE

PATENT INFORMATION:	US 2004038856	A1	20040226
APPLICATION INFO.:	US 2003-440428	A1	20030516 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-381720P	20020517 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: HELLER EHRMAN WHITE & MCAULIFFE LLP, 275 MIDDLEFIELD ROAD, MENLO PARK, CA, 94025-3506
NUMBER OF CLAIMS: 45
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 46 Drawing Page(s)
LINE COUNT: 1787
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention concerns methods of treating fibroproliferative disorders associated with TGF-.beta. signaling, by administering non-peptide small molecule inhibitors of TGF-.beta. specifically binding to the type I TGF-.beta. receptor (TGF.beta.-R1). Preferably, the inhibitors are quinazoline derivatives. The invention also concerns methods for reversing the effect of TGF-.beta.-mediated cell activation on the expression of a gene associated with fibrosis, comprising contacting a cell or tissue in which the expression of such gene is altered as a result of TGF-.beta.-mediated cell activation, with a non-peptide small molecule inhibitor of TGF-.beta., specifically binding a TGF.beta.-R1 receptor kinase present in the cell or tissue.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **40288-70-8 54665-94-0 157862-99-2**
166039-38-9 259870-32-1 259870-33-2
259870-34-3 259870-35-4 259870-36-5
259870-37-6 259870-38-7 259870-39-8
259870-42-3 259870-44-5 404828-44-0
420831-73-8 422561-07-7 438247-46-2
446312-97-6 446829-19-2 474289-34-4
474289-37-7 474289-39-9 474289-40-2
474289-42-4 474289-44-6 474289-46-8
474289-48-0 474289-50-4 474289-54-8
474289-60-6 474289-64-0 474289-68-4
474289-70-8 474289-74-2 474289-76-4
474289-79-7 474289-80-0 474289-82-2
474289-84-4 474289-87-7 474289-89-9
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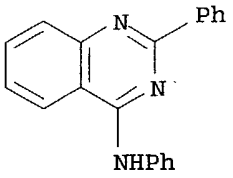
474290-06-7 474290-15-8 474290-17-0
474290-19-2 474290-23-8 474290-26-1
474290-28-3 474290-30-7 627535-94-8
627535-95-9 627535-96-0 627535-97-1
627535-98-2 627535-99-3 627536-02-1
627536-03-2 627536-04-3 627536-05-4
627536-06-5 627536-07-6 627536-08-7
(treatment of fibroproliferative disorders using TGF-.beta. inhibitors)
RN 40288-70-8 USPATFULL
CN 4-Quinazolinamine, N,2-diphenyl- (9CI) (CA INDEX NAME)



RN 54665-94-0 USPATFULL
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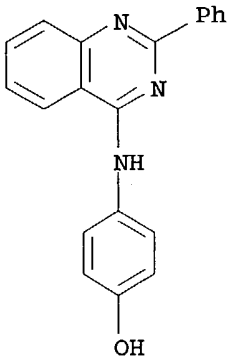
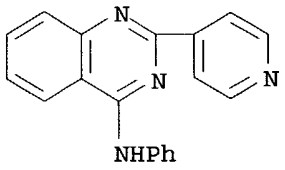
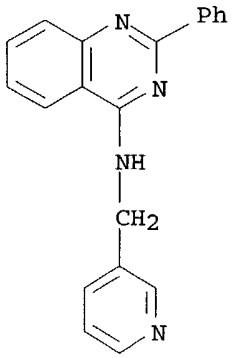


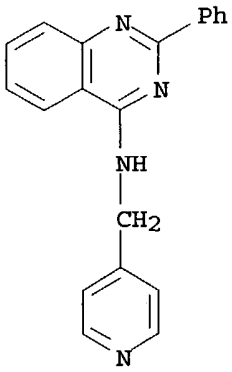
RN 157862-99-2 USPATFULL
CN 4-Quinazolinamine, N-phenyl-2-(4-pyridinyl)- (9CI) (CA INDEX NAME)



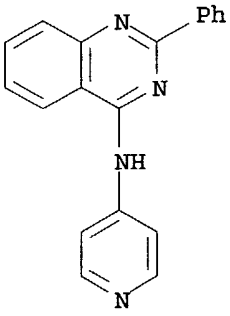
RN 166039-38-9 USPATFULL
CN 4-Quinazolinamine, 2-phenyl-N-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



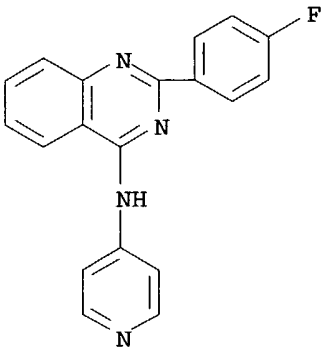
RN 259870-32-1 USPATFULL
CN 4-Quinazolinamine, 2-phenyl-N-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



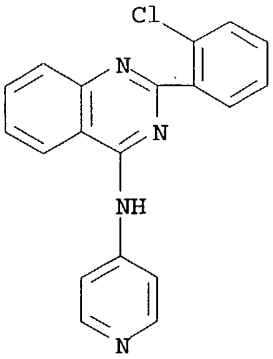
RN 259870-33-2 USPATFULL
CN 4-Quinazolinamine, 2-phenyl-N-4-pyridinyl- (9CI) (CA INDEX NAME)



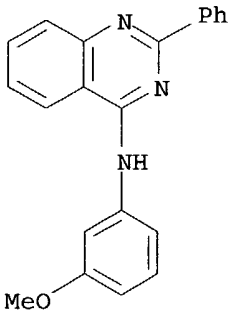
RN 259870-34-3 USPATFULL
CN 4-Quinazolinamine, 2-(4-fluorophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



RN 259870-35-4 USPATFULL
CN 4-Quinazolinamine, 2-(2-chlorophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



RN 259870-36-5 USPATFULL
CN 4-Quinazolinamine, N-(3-methoxyphenyl)-2-phenyl- (9CI) (CA INDEX NAME)



RN 259870-37-6 USPATFULL
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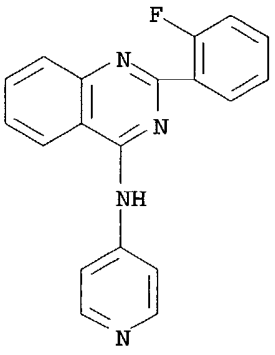
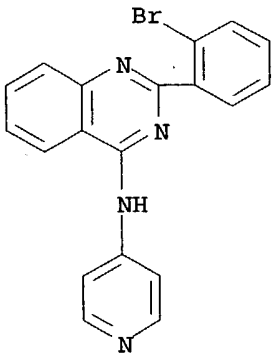
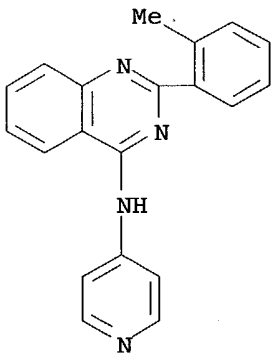


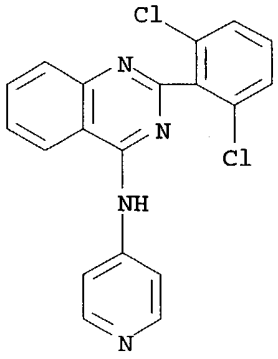
RN 259870-38-7 USPATFULL
CN 4-Quinazolinamine, 2-(2-bromophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



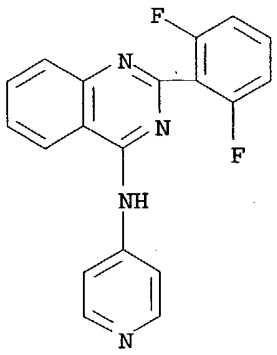
RN 259870-39-8 USPATFULL
CN 4-Quinazolinamine, 2-(2-methylphenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



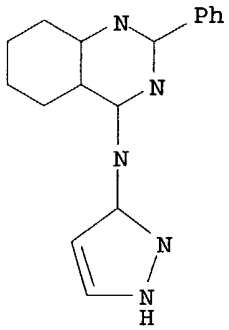
RN 259870-42-3 USPATFULL
CN 4-Quinazolinamine, 2-(2,6-dichlorophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



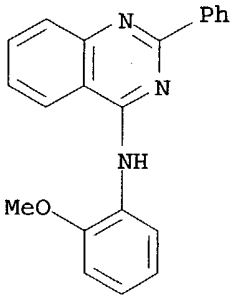
RN 259870-44-5 USPATFULL
CN 4-Quinazolinamine, 2-(2,6-difluorophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



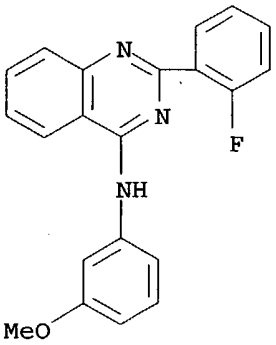
RN 404828-44-0 USPATFULL
CN 4-Quinazolinamine, 2-phenyl-N-1H-pyrazol-3-yl- (9CI) (CA INDEX NAME)



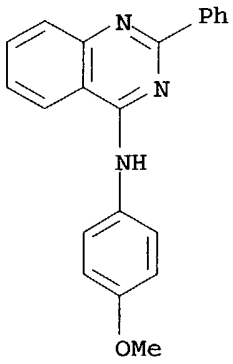
FRAGMENT DIAGRAM IS INCOMPLETE
RN 420831-73-8 USPATFULL
CN 4-Quinazolinamine, N-(2-methoxyphenyl)-2-phenyl- (9CI) (CA INDEX NAME)



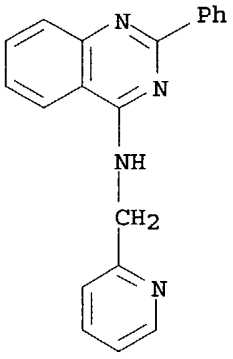
RN 422561-07-7 USPATFULL
CN 4-Quinazolinamine, 2-(2-fluorophenyl)-N-(3-methoxyphenyl)- (9CI) (CA INDEX NAME)



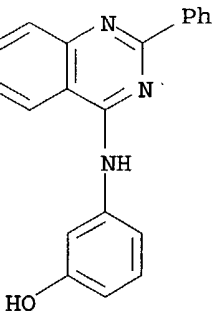
RN 438247-46-2 USPATFULL
CN 4-Quinazolinamine, N-(4-methoxyphenyl)-2-phenyl- (9CI) (CA INDEX NAME)



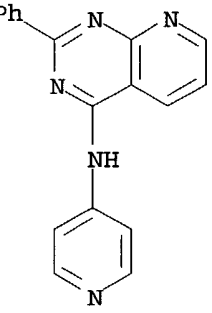
RN 446312-97-6 USPATFULL
CN 4-Quinazolinamine, 2-phenyl-N-(2-pyridinylmethyl)- (9CI) (CA INDEX NAME)



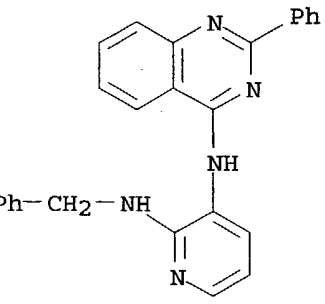
RN 446829-19-2 USPATFULL
CN Phenol, 3-[(2-phenyl-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



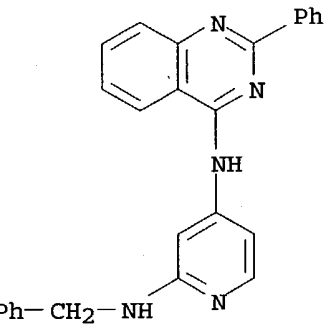
RN 474289-34-4 USPATFULL
CN Pyrido[2,3-d]pyrimidin-4-amine, 2-phenyl-N-4-pyridinyl- (9CI) (CA INDEX NAME)



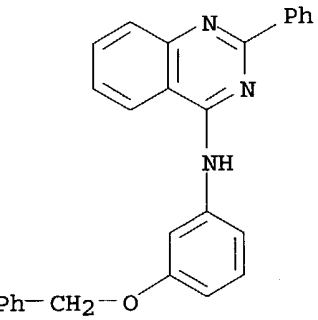
RN 474289-37-7 USPATFULL
CN 2,3-Pyridinediamine, N2-(phenylmethyl)-N3-(2-phenyl-4-quinazolinyl)- (9CI) (CA INDEX NAME)



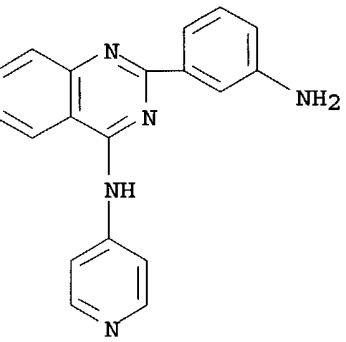
RN 474289-39-9 USPATFULL
CN 2,4-Pyridinediamine, N2-(phenylmethyl)-N4-(2-phenyl-4-quinazolinyl)- (9CI) (CA INDEX NAME)



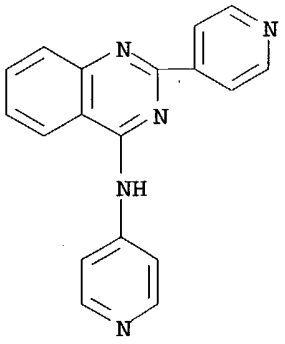
RN 474289-40-2 USPATFULL
CN 4-Quinazolinamine, 2-phenyl-N-[3-(phenylmethoxy)phenyl]- (9CI) (CA INDEX NAME)



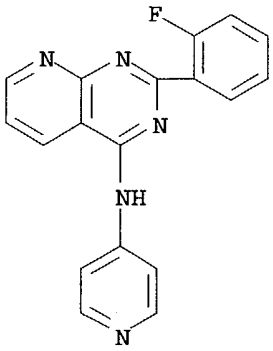
RN 474289-42-4 USPATFULL
CN 4-Quinazolinamine, 2-(3-aminophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



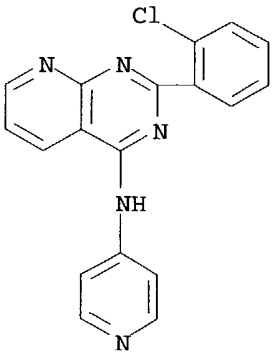
RN 474289-44-6 USPATFULL
CN 4-Quinazolinamine, N,2-di-4-pyridinyl- (9CI) (CA INDEX NAME)



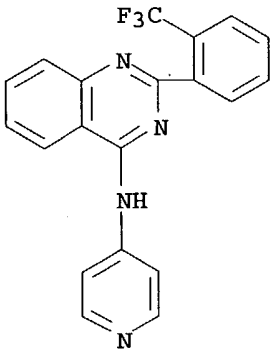
RN 474289-46-8 USPATFULL
CN Pyrido[2,3-d]pyrimidin-4-amine, 2-(2-fluorophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



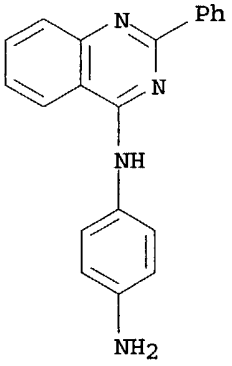
RN 474289-48-0 USPATFULL
CN Pyrido[2,3-d]pyrimidin-4-amine, 2-(2-chlorophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



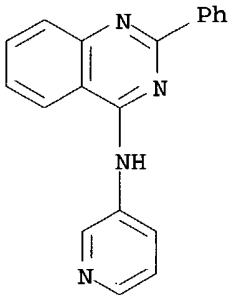
RN 474289-50-4 USPATFULL
CN 4-Quinazolinamine, N-4-pyridinyl-2-[2-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



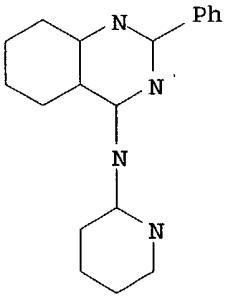
RN 474289-54-8 USPATFULL
CN 1,4-Benzenediamine, N-(2-phenyl-4-quinazolinyl)- (9CI) (CA INDEX NAME)



RN 474289-60-6 USPATFULL
CN 4-Quinazolinamine, 2-phenyl-N-3-pyridinyl- (9CI) (CA INDEX NAME)

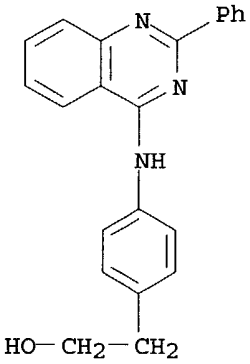


RN 474289-64-0 USPATFULL
CN 4-Quinazolinamine, 2-phenyl-N-2-pyridinyl- (9CI) (CA INDEX NAME)

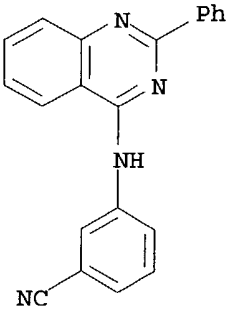


FRAGMENT DIAGRAM IS INCOMPLETE

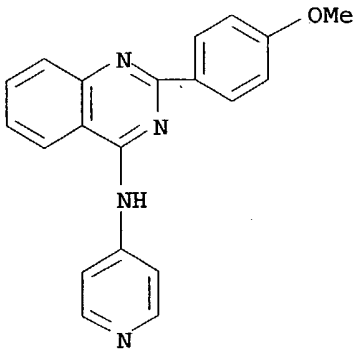
RN 474289-68-4 USPATFULL
CN Benzeneethanol, 4-[(2-phenyl-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



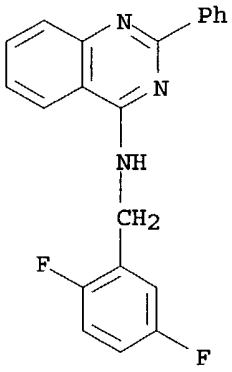
RN 474289-70-8 USPATFULL
CN Benzonitrile, 3-[(2-phenyl-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



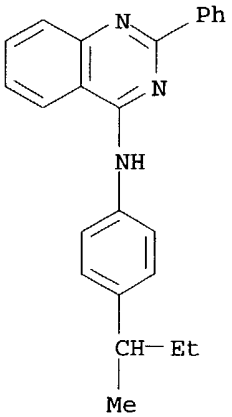
RN 474289-74-2 USPATFULL
CN 4-Quinazolinamine, 2-(4-methoxyphenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



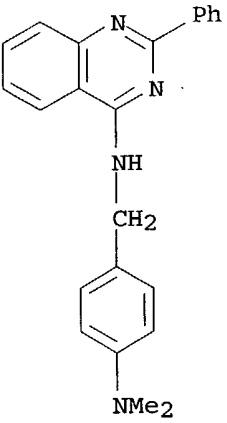
RN 474289-76-4 USPATFULL
CN 4-Quinazolinamine, N-[(2,5-difluorophenyl)methyl]-2-phenyl- (9CI) (CA INDEX NAME)



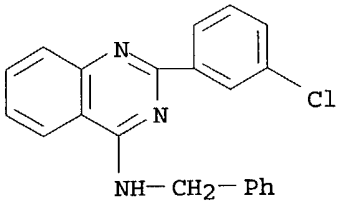
RN 474289-79-7 USPATFULL
CN 4-Quinazolinamine, N-[4-(1-methylpropyl)phenyl]-2-phenyl- (9CI) (CA INDEX NAME)



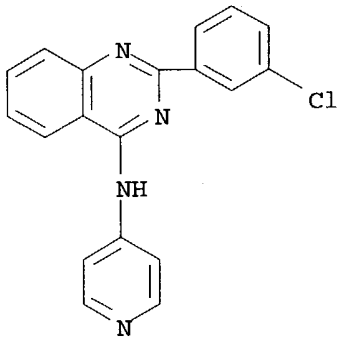
RN 474289-80-0 USPATFULL
CN 4-Quinazolinamine, N-[[4-(dimethylamino)phenyl]methyl]-2-phenyl- (9CI) (CA INDEX NAME)



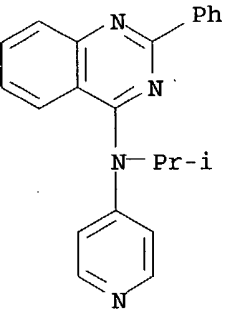
RN 474289-82-2 USPATFULL
CN 4-Quinazolinamine, 2-(3-chlorophenyl)-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



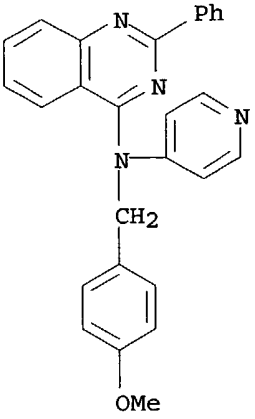
RN 474289-84-4 USPATFULL
CN 4-Quinazolinamine, 2-(3-chlorophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



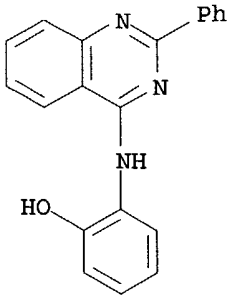
RN 474289-87-7 USPATFULL
CN 4-Quinazolinamine, N-(1-methylethyl)-2-phenyl-N-4-pyridinyl- (9CI) (CA INDEX NAME)



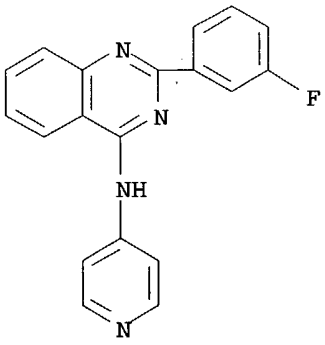
RN 474289-89-9 USPATFULL
CN 4-Quinazolinamine, N-[(4-methoxyphenyl)methyl]-2-phenyl-N-4-pyridinyl- (9CI) (CA INDEX NAME)



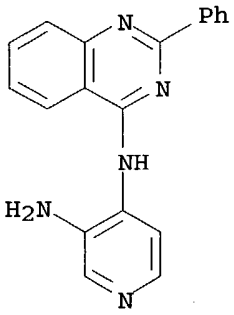
RN 474289-93-5 USPATFULL
CN Phenol, 2-[(2-phenyl-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



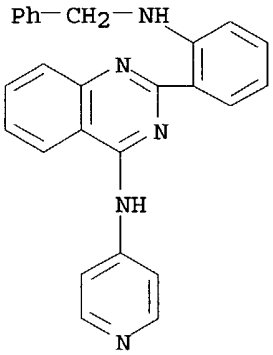
RN 474289-98-0 USPATFULL
CN 4-Quinazolinamine, 2-(3-fluorophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



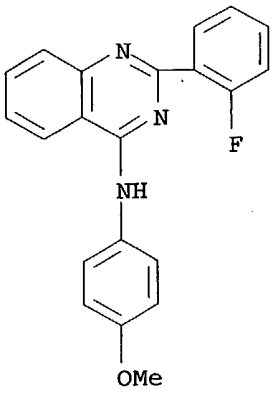
RN 474290-04-5 USPATFULL
CN 3,4-Pyridinediamine, N4-(2-phenyl-4-quinazolinyl)- (9CI) (CA INDEX NAME)



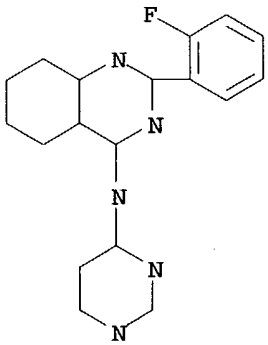
RN 474290-06-7 USPATFULL
CN 4-Quinazolinamine, 2-[2-[(phenylmethyl)amino]phenyl]-N-4-pyridinyl- (9CI) (CA INDEX NAME)



RN 474290-15-8 USPATFULL
CN 4-Quinazolinamine, 2-(2-fluorophenyl)-N-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

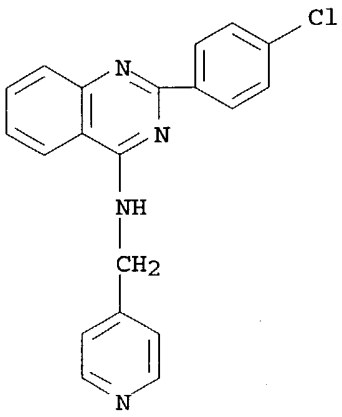


RN 474290-17-0 USPATFULL
CN 4-Quinazolinamine, 2-(2-fluorophenyl)-N-4-pyrimidinyl- (9CI) (CA INDEX NAME)

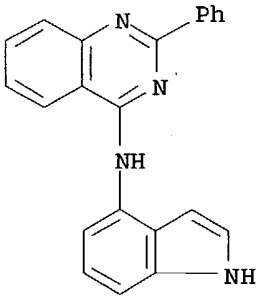


FRAGMENT DIAGRAM IS INCOMPLETE

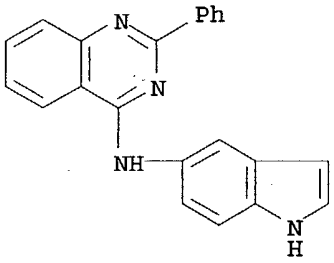
RN 474290-19-2 USPATFULL
CN 4-Quinazolinamine, 2-(4-chlorophenyl)-N-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



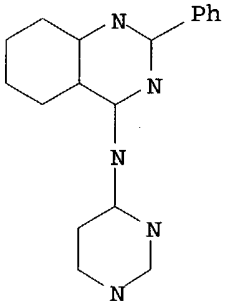
RN 474290-23-8 USPATFULL
CN 4-Quinazolinamine, N-1H-indol-4-yl-2-phenyl- (9CI) (CA INDEX NAME)



RN 474290-26-1 USPATFULL
CN 4-Quinazolinamine, N-1H-indol-5-yl-2-phenyl- (9CI) (CA INDEX NAME)

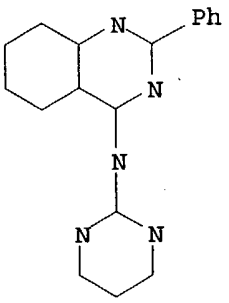


RN 474290-28-3 USPATFULL
CN 4-Quinazolinamine, 2-phenyl-N-4-pyrimidinyl- (9CI) (CA INDEX NAME)



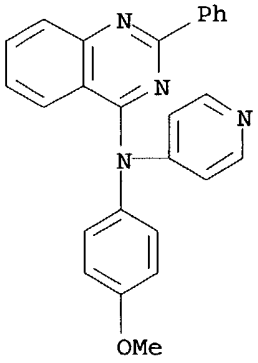
FRAGMENT DIAGRAM IS INCOMPLETE

RN 474290-30-7 USPATFULL
CN 4-Quinazolinamine, 2-phenyl-N-2-pyrimidinyl- (9CI) (CA INDEX NAME)

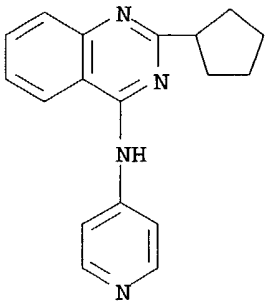


FRAGMENT DIAGRAM IS INCOMPLETE

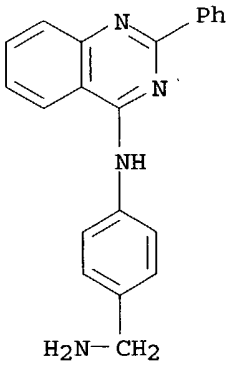
RN 627535-94-8 USPATFULL
CN 4-Quinazolinamine, N-(4-methoxyphenyl)-2-phenyl-N-4-pyridinyl- (9CI) (CA INDEX NAME)



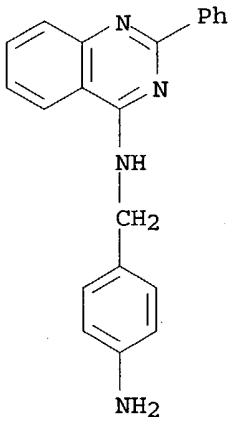
RN 627535-95-9 USPATFULL
CN 4-Quinazolinamine, 2-cyclopentyl-N-4-pyridinyl- (9CI) (CA INDEX NAME)



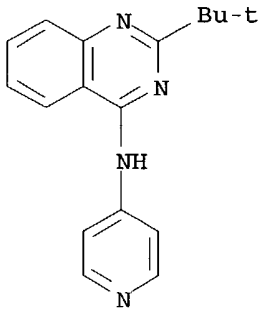
RN 627535-96-0 USPATFULL
CN 4-Quinazolinamine, N-[4-(aminomethyl)phenyl]-2-phenyl- (9CI) (CA INDEX NAME)



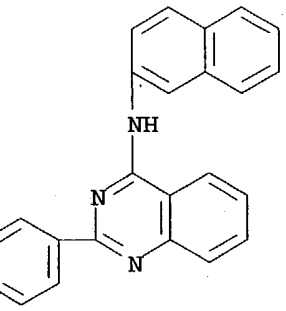
RN 627535-97-1 USPATFULL
CN 4-Quinazolinamine, N-[(4-aminophenyl)methyl]-2-phenyl- (9CI) (CA INDEX NAME)



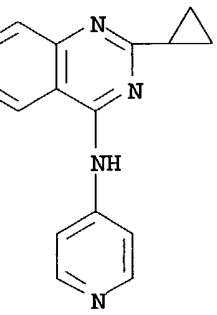
RN 627535-98-2 USPATFULL
CN 4-Quinazolinamine, 2-(1,1-dimethylethyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



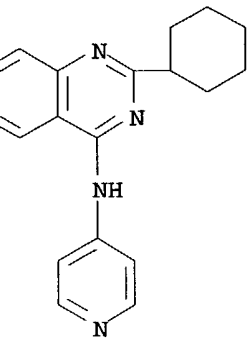
RN 627535-99-3 USPATFULL
CN 4-Quinazolinamine, N-2-naphthalenyl-2-(4-pyridinyl)- (9CI) (CA INDEX NAME)



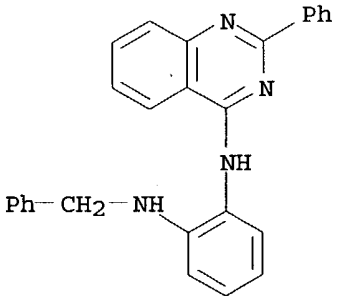
N 627536-02-1 USPATFULL
N 4-Quinazolinamine, 2-cyclopropyl-N-4-pyridinyl- (9CI) (CA INDEX NAME)



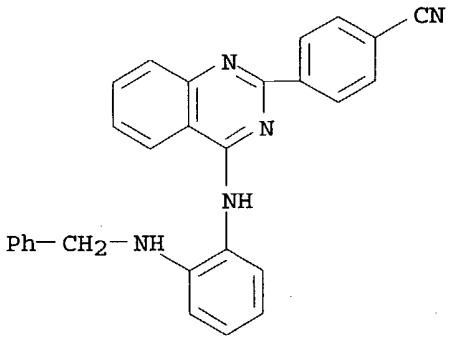
N 627536-03-2 USPATFULL
N 4-Quinazolinamine, 2-cyclohexyl-N-4-pyridinyl- (9CI) (CA INDEX NAME)



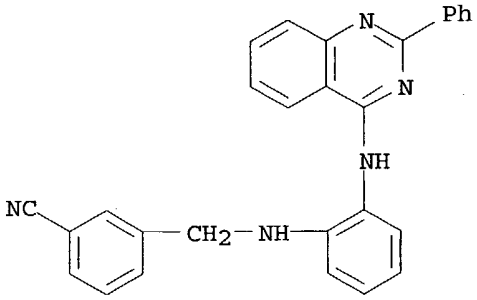
N 627536-04-3 USPATFULL
N 1,2-Benzenediamine, N-(phenylmethyl)-N'-(2-phenyl-4-quinazolinyl)- (9CI)
(CA INDEX NAME)



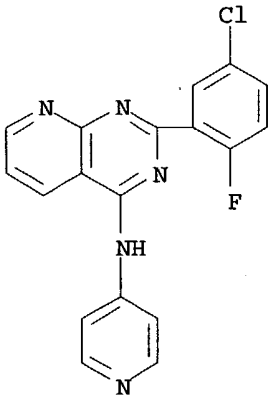
RN 627536-05-4 USPATFULL
CN Benzonitrile, 4-[4-[[2-[(phenylmethyl)amino]phenyl]amino]-2-quinazolinyl]-
(9CI) (CA INDEX NAME)



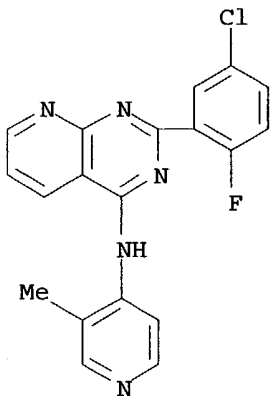
RN 627536-06-5 USPATFULL
CN Benzonitrile, 3-[[[2-[(2-phenyl-4-quinazolinyl)amino]phenyl]amino]methyl]-
(9CI) (CA INDEX NAME)



RN 627536-07-6 USPATFULL
CN Pyrido[2,3-d]pyrimidin-4-amine, 2-(5-chloro-2-fluorophenyl)-N-4-pyridinyl-
(9CI) (CA INDEX NAME)



RN 627536-08-7 USPATFULL
CN Pyrido[2,3-d]pyrimidin-4-amine, 2-(5-chloro-2-fluorophenyl)-N-(3-methyl-4-pyridinyl)- (9CI) (CA INDEX NAME)



L41 ANSWER 20 OF 37 USPATFULL on STN
ACCESSION NUMBER: 2003:330180 USPATFULL
TITLE: Identification of kinase inhibitors
INVENTOR(S): Prescott, John C., San Francisco, CA, UNITED STATES
Braisted, Andrew, San Francisco, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003232391	A1	20031218
APPLICATION INFO.:	US 2003-394322	A1	20030320 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-366892P	20020321 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: HELLER EHRMAN WHITE & MCAULIFFE LLP, 275 MIDDLEFIELD ROAD, MENLO PARK, CA, 94025-3506
NUMBER OF CLAIMS: 76
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 2 Drawing Page(s)
LINE COUNT: 9497
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

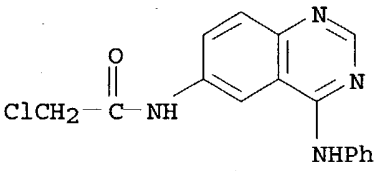
AB The invention concerns the identification of protein kinase inhibitors that preferentially bind to the inactive conformation of a target protein kinase. The inhibitors are identified by locking the target protein kinase in an inactive conformation, and using a covalent tethering approach to identify inhibitors preferentially targeting the inactive conformation.

CROSS-REFERENCE TO RELATED APPLICATION

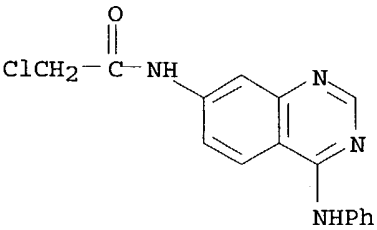
This application claims the benefit of U.S. Provisional Patent Application No. 60/366,892, filed Mar. 21, 2002 which is incorporated herein by reference.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **165245-96-5**, Protein kinase RK **608121-96-6**
608121-97-7 608121-98-8 608121-99-9
608122-00-5 608122-01-6 608122-02-7
608122-03-8 608122-04-9 608122-05-0
608122-06-1 608122-07-2 608122-08-3
608122-09-4 608122-10-7 608122-11-8
608122-12-9
(method for identification of kinase inhibitors using covalent tethering of ligands to kinase locked in inactive conformation)
RN 165245-96-5 USPATFULL
CN Kinase (phosphorylating), protein, RK (9CI) (CA INDEX NAME)

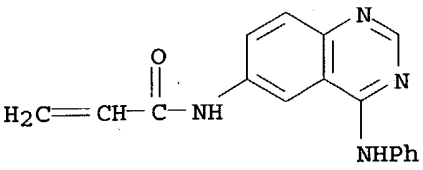
STRUCTURE DIAGRAM IS NOT AVAILABLE
RN 608121-96-6 USPATFULL
CN Acetamide, 2-chloro-N-[4-(phenylamino)-6-quinazolinyl]- (9CI) (CA INDEX NAME)



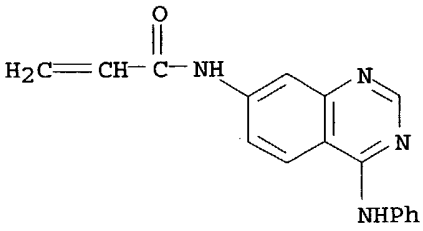
RN 608121-97-7 USPATFULL
CN Acetamide, 2-chloro-N-[4-(phenylamino)-7-quinazolinyl]- (9CI) (CA INDEX NAME)



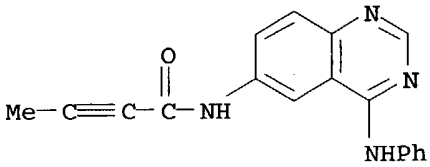
RN 608121-98-8 USPATFULL
CN 2-Propenamide, N-[4-(phenylamino)-6-quinazolinyl]- (9CI) (CA INDEX NAME)



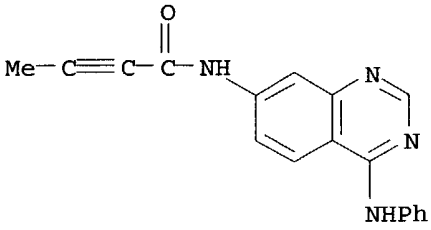
RN 608121-99-9 USPATFULL
CN 2-Propenamide, N-[4-(phenylamino)-7-quinazolinyl]- (9CI) (CA INDEX NAME)



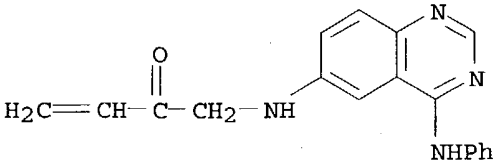
RN 608122-00-5 USPATFULL
CN 2-Butynamide, N-[4-(phenylamino)-6-quinazolinyl]- (9CI) (CA INDEX NAME)



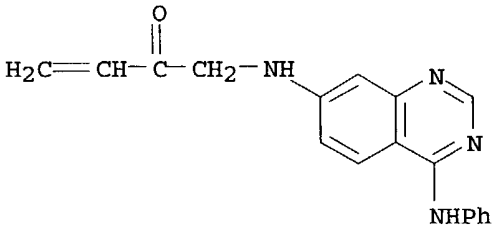
RN 608122-01-6 USPATFULL
CN 2-Butynamide, N-[4-(phenylamino)-7-quinazolinyl]- (9CI) (CA INDEX NAME)



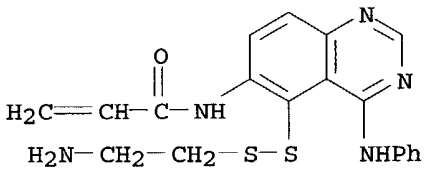
RN 608122-02-7 USPATFULL
CN 3-Buten-2-one, 1-[[4-(phenylamino)-6-quinazolinyl]amino]- (9CI) (CA INDEX NAME)



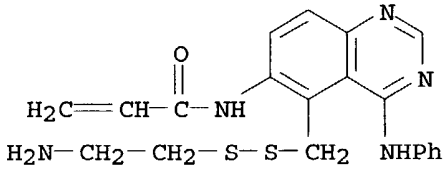
RN 608122-03-8 USPATFULL
CN 3-Buten-2-one, 1-[[4-(phenylamino)-7-quinazolinyl]amino]- (9CI) (CA INDEX NAME)



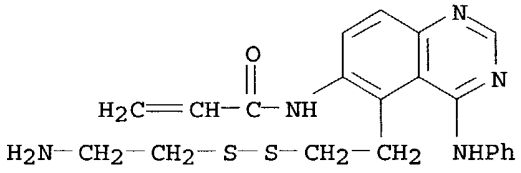
RN 608122-04-9 USPATFULL
CN 2-Propenamide, N-[5-[(2-aminoethyl)dithio]-4-(phenylamino)-6-quinazolinyl]- (9CI) (CA INDEX NAME)



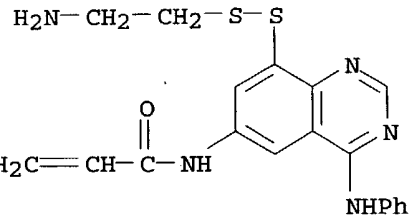
RN 608122-05-0 USPATFULL
CN 2-Propenamide, N-[5-[[(2-aminoethyl)dithio]methyl]-4-(phenylamino)-6-quinazolinyl]- (9CI) (CA INDEX NAME)



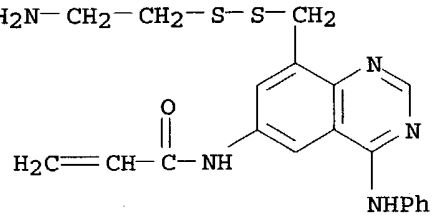
RN 608122-06-1 USPATFULL
CN 2-Propenamide, N-[5-[2-[(2-aminoethyl)dithio]ethyl]-4-(phenylamino)-6-quinazolinyl]- (9CI) (CA INDEX NAME)



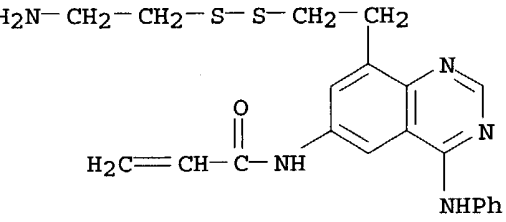
RN 608122-07-2 USPATFULL
CN 2-Propenamide, N-[8-[(2-aminoethyl)dithio]-4-(phenylamino)-6-quinazolinyl]- (9CI) (CA INDEX NAME)



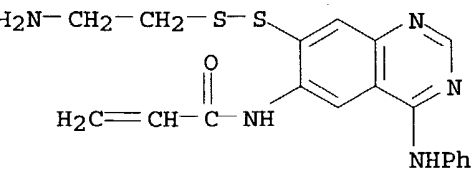
RN 608122-08-3 USPATFULL
CN 2-Propenamide, N-[8-[[(2-aminoethyl)dithio]methyl]-4-(phenylamino)-6-quinazolinyl]- (9CI) (CA INDEX NAME)



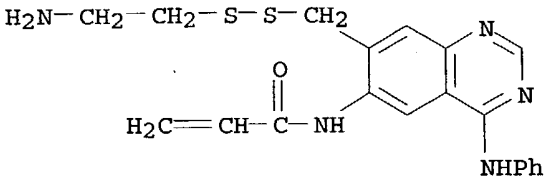
RN 608122-09-4 USPATFULL
CN 2-Propenamide, N-[8-[2-[(2-aminoethyl)dithio]ethyl]-4-(phenylamino)-6-quinazolinyl]- (9CI) (CA INDEX NAME)



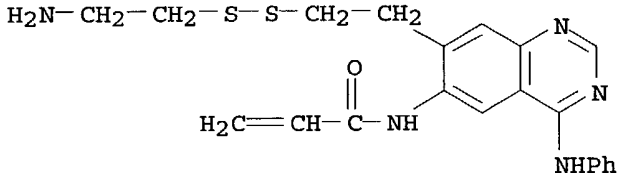
RN 608122-10-7 USPATFULL
CN 2-Propenamide, N-[7-[(2-aminoethyl)dithio]-4-(phenylamino)-6-quinazolinyl]- (9CI) (CA INDEX NAME)



RN 608122-11-8 USPATFULL
CN 2-Propenamide, N-[7-[[(2-aminoethyl)dithio]methyl]-4-(phenylamino)-6-quinazolinyl]- (9CI) , (CA INDEX NAME)



RN 608122-12-9 USPATFULL
CN 2-Propenamide, N-[7-[2-[(2-aminoethyl)dithio]ethyl]-4-(phenylamino)-6-quinazolinyl]- (9CI) (CA INDEX NAME)



L41 ANSWER 21 OF 37 USPATFULL on STN
ACCESSION NUMBER: 2003:100137 USPATFULL
TITLE: Quinazoline derivatives as medicaments
INVENTOR(S): Chakravarty, Sarvajit, Sunnyvale, CA, UNITED STATES
Dugar, Sundeep, Bridgewater, NJ, UNITED STATES
Perumattam, John J., Los Altos, CA, UNITED STATES
Schreiner, George F., Los Altos Hills, CA, UNITED STATES
Liu, David Y., Palo Alto, CA, UNITED STATES
Lewicki, John A., Los Gatos, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003069248	A1	20030410
APPLICATION INFO.:	US 2001-969936	A1	20011002 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1999-383825, filed on 27 Aug 1999, PENDING Continuation-in-part of Ser. No. US 1998-141916, filed on 28 Aug 1998, GRANTED, Pat. No. US 6184226
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MORRISON & FOERSTER LLP, 3811 VALLEY CENTRE DRIVE, SUITE 500, SAN DIEGO, CA, 92130-2332
NUMBER OF CLAIMS: 22
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 10 Drawing Page(s)
LINE COUNT: 1336
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention is directed to methods to inhibit TGF-.beta.and/or **p38-.alpha. kinase** using compounds of the formula ##STR1##

or the pharmaceutically acceptable salts thereof

wherein R.sup.3 is a noninterfering substituent;

each Z is CR.sup.2 or N, wherein no more than two Z positions in ring A

are N, and wherein two adjacent Z positions in ring A cannot be N;

each R.sup.2 is independently a noninterfering substituent;

L is a linker;

n is 0 or 1;and

Ar' is the residue of a cyclic aliphatic, cyclic heteroaliphatic, aromatic or heteroaromatic moiety optionally substituted with 1-3 noninterfering substituents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT **165245-96-5**
(mediated disorders; treatment; prepn. of quinazolines as **p38 -.alpha. kinase** and TGF-.beta. inhibitors)

RN 165245-96-5 USPATFULL

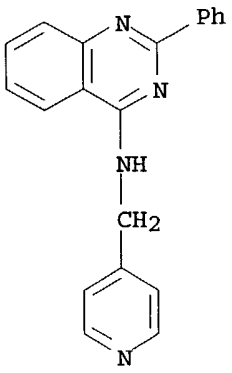
CN Kinase (phosphorylating), protein, RK (9CI) (CA INDEX NAME)

STRUCTURE DIAGRAM IS NOT AVAILABLE

IT **259870-32-1P 259870-33-2P 259870-34-3P**
259870-35-4P 259870-36-5P 259870-37-6P
259870-38-7P 259870-39-8P 259870-40-1P
259870-41-2P 259870-42-3P 259870-43-4P
259870-44-5P 259870-45-6P 259870-46-7P
259870-47-8P 259870-48-9P 259870-49-0P
259870-50-3P 259870-51-4P 259870-52-5P
(prepn. of quinazolines as **p38-.alpha. kinase** and TGF-.beta. inhibitors)

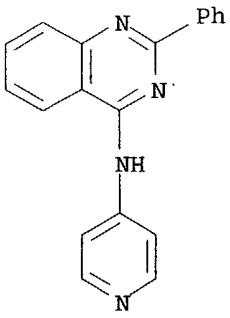
RN 259870-32-1 USPATFULL

CN 4-Quinazolinamine, 2-phenyl-N-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)

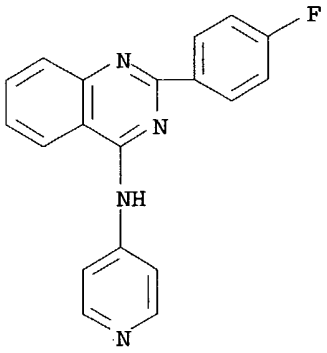


RN 259870-33-2 USPATFULL

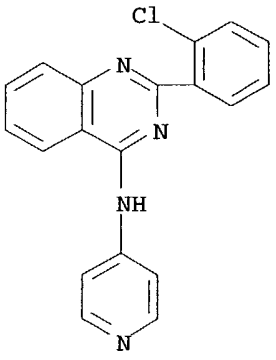
CN 4-Quinazolinamine, 2-phenyl-N-4-pyridinyl- (9CI) (CA INDEX NAME)



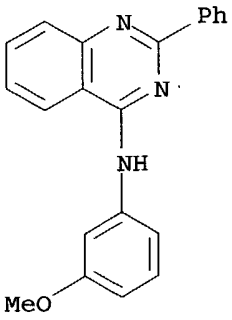
RN 259870-34-3 USPATFULL
CN 4-Quinazolinamine, 2-(4-fluorophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



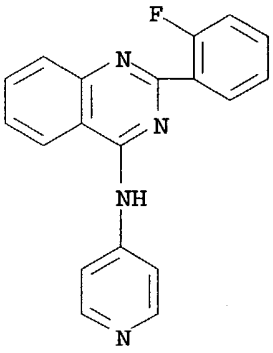
RN 259870-35-4 USPATFULL
CN 4-Quinazolinamine, 2-(2-chlorophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



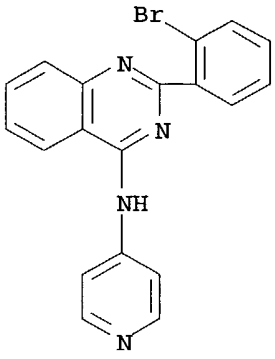
RN 259870-36-5 USPATFULL
CN 4-Quinazolinamine, N-(3-methoxyphenyl)-2-phenyl- (9CI) (CA INDEX NAME)



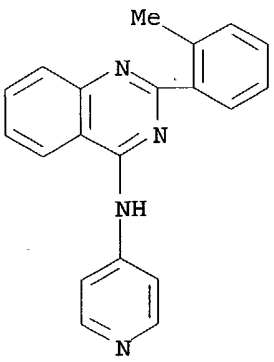
RN 259870-37-6 USPATFULL
CN 4-Quinazolinamine, 2-(2-fluorophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



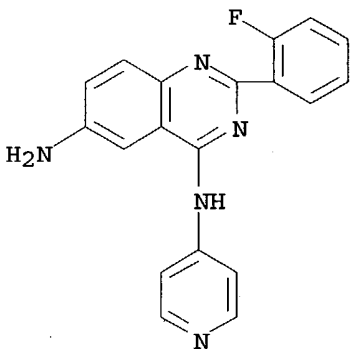
RN 259870-38-7 USPATFULL
CN 4-Quinazolinamine, 2-(2-bromophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



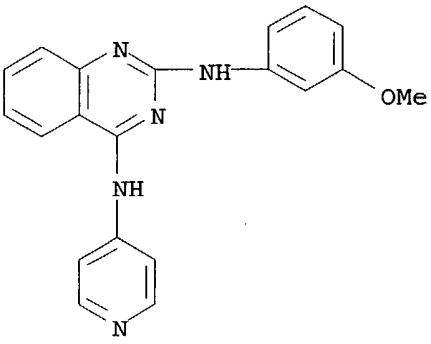
RN 259870-39-8 USPATFULL
CN 4-Quinazolinamine, 2-(2-methylphenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



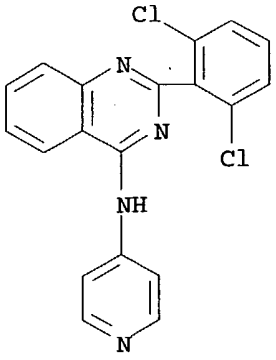
RN 259870-40-1 USPATFULL
CN 4,6-Quinazolinediamine, 2-(2-fluorophenyl)-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



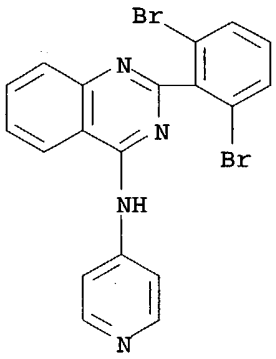
RN 259870-41-2 USPATFULL
CN 2,4-Quinazolinediamine, N2-(3-methoxyphenyl)-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



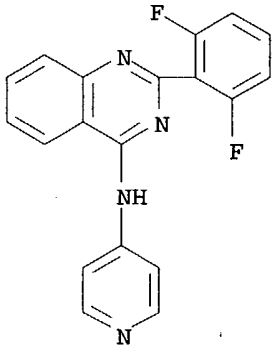
RN 259870-42-3 USPATFULL
CN 4-Quinazolinamine, 2-(2,6-dichlorophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



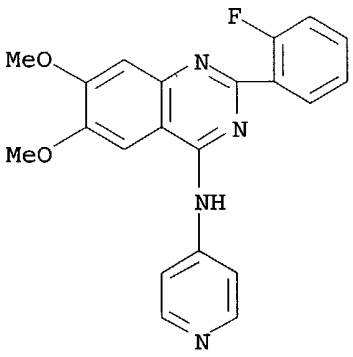
RN 259870-43-4 USPATFULL
CN 4-Quinazolinamine, 2-(2,6-dibromophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



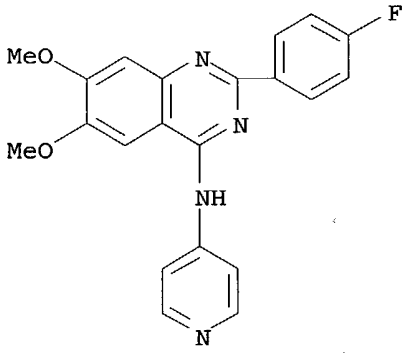
RN 259870-44-5 USPATFULL
CN 4-Quinazolinamine, 2-(2,6-difluorophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



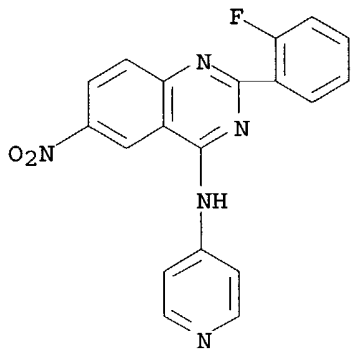
RN 259870-45-6 USPATFULL
CN 4-Quinazolinamine, 2-(2-fluorophenyl)-6,7-dimethoxy-N-4-pyridinyl- (9CI) (CA INDEX NAME)



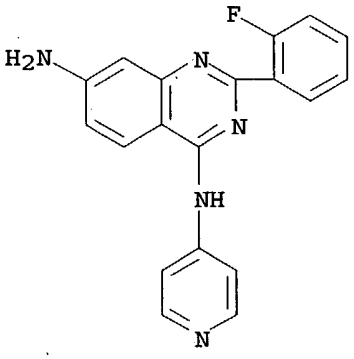
RN 259870-46-7 USPATFULL
CN 4-Quinazolinamine, 2-(4-fluorophenyl)-6,7-dimethoxy-N-4-pyridinyl- (9CI) (CA INDEX NAME)



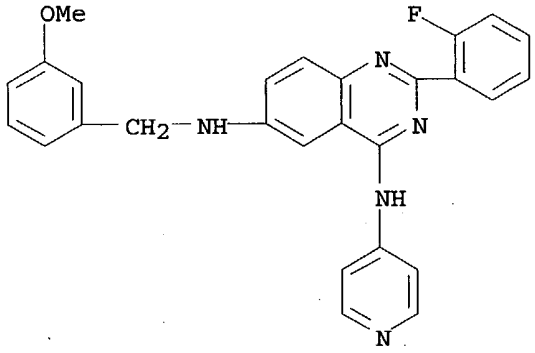
RN 259870-47-8 USPATFULL
CN 4-Quinazolinamine, 2-(2-fluorophenyl)-6-nitro-N-4-pyridinyl- (9CI) (CA INDEX NAME)



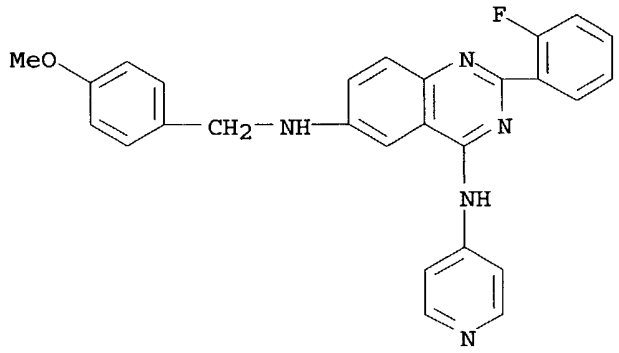
RN 259870-48-9 USPATFULL
CN 4,7-Quinazolinediamine, 2-(2-fluorophenyl)-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



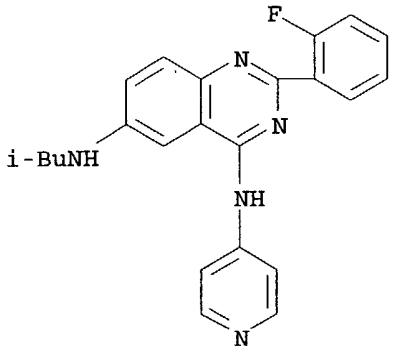
RN 259870-49-0 USPATFULL
CN 4,6-Quinazolinediamine, 2-(2-fluorophenyl)-N6-[(3-methoxyphenyl)methyl]-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



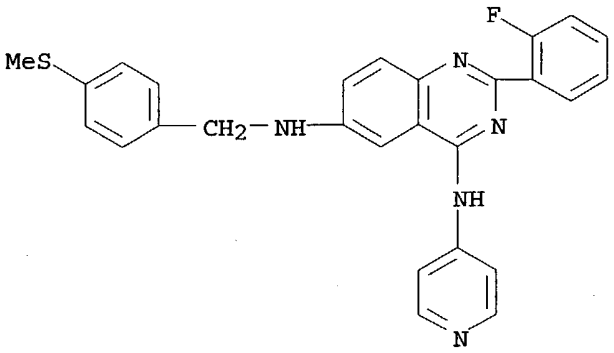
RN 259870-50-3 USPATFULL
CN 4,6-Quinazolinediamine, 2-(2-fluorophenyl)-N6-[(4-methoxyphenyl)methyl]-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



RN 259870-51-4 USPATFULL
CN 4,6-Quinazolinediamine, 2-(2-fluorophenyl)-N6-(2-methylpropyl)-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



RN 259870-52-5 USPATFULL
CN 4,6-Quinazolinediamine, 2-(2-fluorophenyl)-N6-[[4-(methylthio)phenyl]methyl]-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



L41 ANSWER 22 OF 37 USPATFULL on STN

ACCESSION NUMBER:	2002:288140 USPATFULL
TITLE:	Quinazoline derivatives as medicaments
INVENTOR(S):	Chakravarty, Sarvajit, Sunnyvale, CA, UNITED STATES Dugar, Sundeep, Bridgewater, NJ, UNITED STATES Perumattam, John J., Los Altos, CA, UNITED STATES Schreiner, George F., Los Altos Hills, CA, UNITED STATES Liu, David Y., Palo Alto, CA, UNITED STATES Lewicki, John A., Los Gatos, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002161010	A1	20021031
APPLICATION INFO.:	US 2001-972582	A1	20011005 (9)

RELATED APPLN. INFO.:	Continuation of Ser. No. US 1999-383825, filed on 27 Aug 1999, PENDING Continuation-in-part of Ser. No. US 1998-141916, filed on 28 Aug 1998, GRANTED, Pat. No. US 6184226
DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	MORRISON & FOERSTER LLP, 3811 VALLEY CENTRE DRIVE, SUITE 500, SAN DIEGO, CA, 92130-2332
NUMBER OF CLAIMS:	22
EXEMPLARY CLAIM:	1

NUMBER OF DRAWINGS: 10 Drawing Page(s)
LINE COUNT: 1315
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention is directed to methods to inhibit TGF-.beta. and/or **p38-.alpha. kinase** using compounds of the formula ##STR1##

or the pharmaceutically acceptable salts thereof

wherein R.sup.3 is a noninterfering substituent;

each Z is CR.sup.2 or N, wherein no more than two Z positions in ring A are N, and

wherein two adjacent Z positions in ring A cannot be N;

each R.sup.2 is independently a noninterfering substituent;

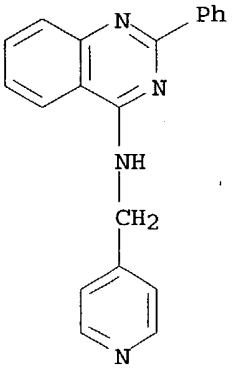
L is a linker;

n is 0 or 1 ; and

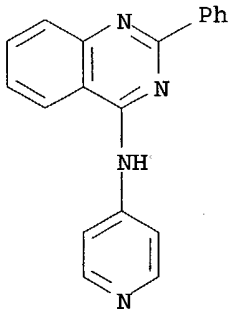
Ar' is the residue of a cyclic aliphatic, cyclic heteroaliphatic, aromatic or heteroaromatic moiety optionally substituted with 1-3 noninterfering substituents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **165245-96-5**
(mediated disorders; treatment; prepn. of quinazolines as **p38 -.alpha. kinase** and TGF-.beta. inhibitors)
RN 165245-96-5 USPATFULL
CN Kinase (phosphorylating), protein, RK (9CI) (CA INDEX NAME)

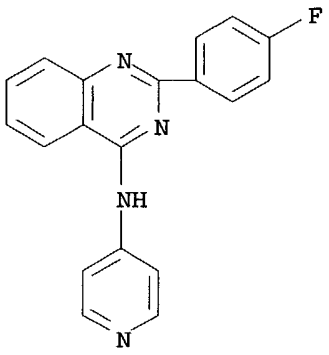
STRUCTURE DIAGRAM IS NOT AVAILABLE
IT **259870-32-1P 259870-33-2P 259870-34-3P**
259870-35-4P 259870-36-5P 259870-37-6P
259870-38-7P 259870-39-8P 259870-40-1P
259870-41-2P 259870-42-3P 259870-43-4P
259870-44-5P 259870-45-6P 259870-46-7P
259870-47-8P 259870-48-9P 259870-49-0P
259870-50-3P 259870-51-4P 259870-52-5P
(prepn. of quinazolines as **p38-.alpha. kinase** and TGF-.beta. inhibitors)
RN 259870-32-1 USPATFULL
CN 4-Quinazolinamine, 2-phenyl-N-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



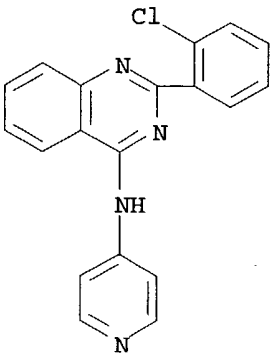
RN 259870-33-2 USPATFULL
CN 4-Quinazolinamine, 2-phenyl-N-4-pyridinyl- (9CI) (CA INDEX NAME)



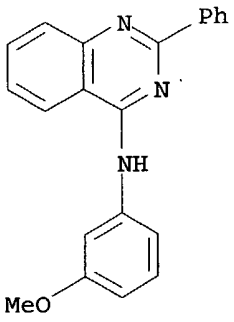
RN 259870-34-3 USPATFULL
CN 4-Quinazolinamine, 2-(4-fluorophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



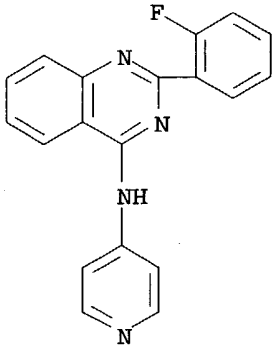
RN 259870-35-4 USPATFULL
CN 4-Quinazolinamine, 2-(2-chlorophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



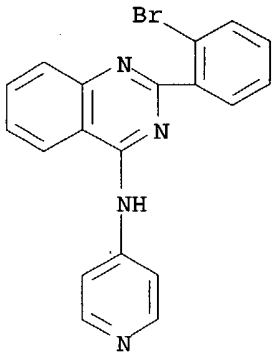
RN 259870-36-5 USPATFULL
CN 4-Quinazolinamine, N-(3-methoxyphenyl)-2-phenyl- (9CI) (CA INDEX NAME)



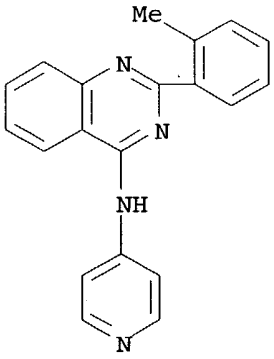
RN 259870-37-6 USPATFULL
CN 4-Quinazolinamine, 2-(2-fluorophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



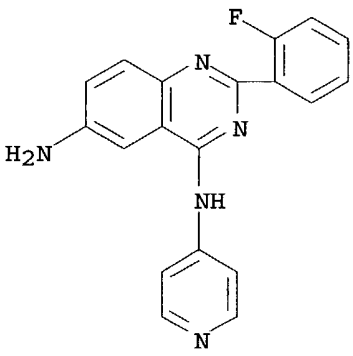
RN 259870-38-7 USPATFULL
CN 4-Quinazolinamine, 2-(2-bromophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



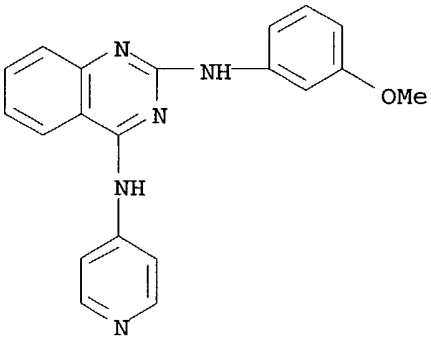
RN 259870-39-8 USPATFULL
CN 4-Quinazolinamine, 2-(2-methylphenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



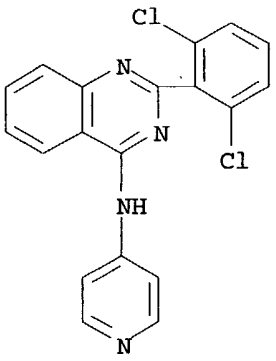
RN 259870-40-1 USPATFULL
CN 4,6-Quinazolinediamine, 2-(2-fluorophenyl)-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



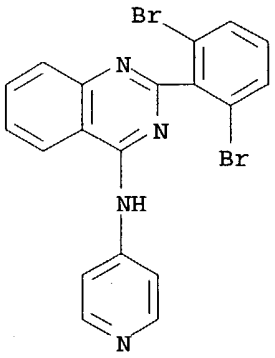
RN 259870-41-2 USPATFULL
CN 2,4-Quinazolinediamine, N2-(3-methoxyphenyl)-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



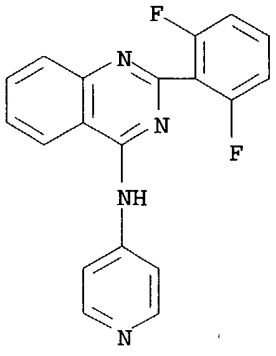
RN 259870-42-3 USPATFULL
CN 4-Quinazolinamine, 2-(2,6-dichlorophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



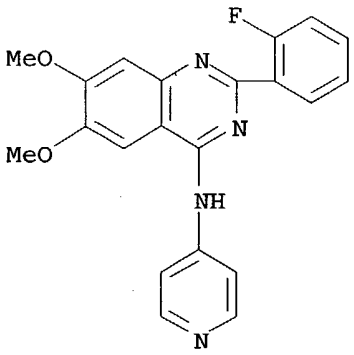
RN 259870-43-4 USPATFULL
CN 4-Quinazolinamine, 2-(2,6-dibromophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



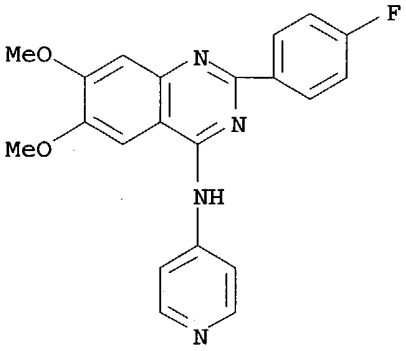
RN 259870-44-5 USPATFULL
CN 4-Quinazolinamine, 2-(2,6-difluorophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



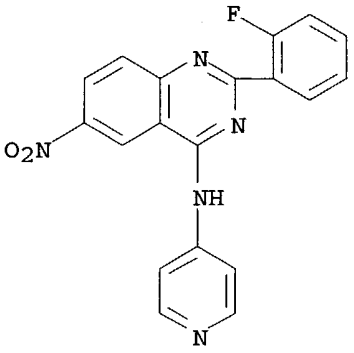
RN 259870-45-6 USPATFULL
CN 4-Quinazolinamine, 2-(2-fluorophenyl)-6,7-dimethoxy-N-4-pyridinyl- (9CI) (CA INDEX NAME)



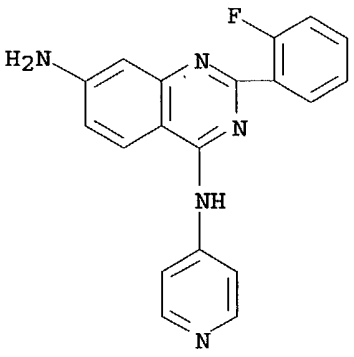
RN 259870-46-7 USPATFULL
CN 4-Quinazolinamine, 2-(4-fluorophenyl)-6,7-dimethoxy-N-4-pyridinyl- (9CI) (CA INDEX NAME)



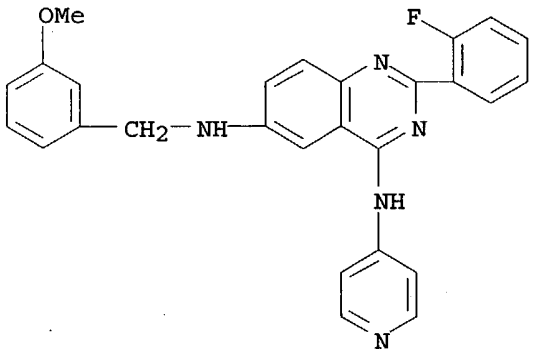
RN 259870-47-8 USPATFULL
CN 4-Quinazolinamine, 2-(2-fluorophenyl)-6-nitro-N-4-pyridinyl- (9CI) (CA INDEX NAME)



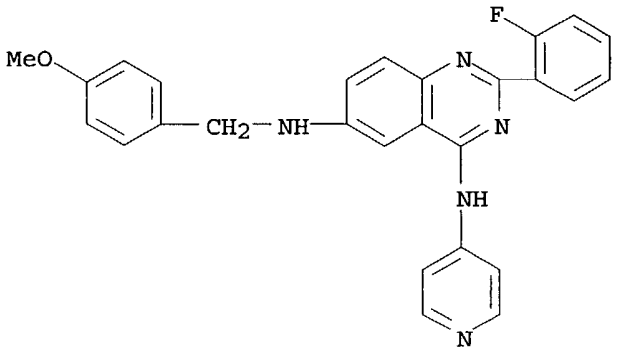
RN 259870-48-9 USPATFULL
CN 4,7-Quinazolinediamine, 2-(2-fluorophenyl)-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



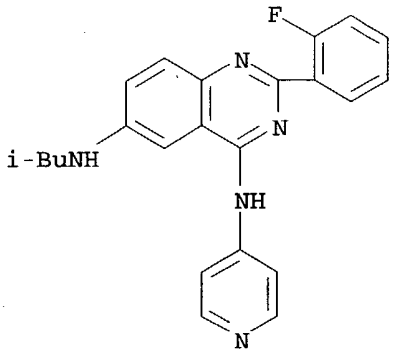
RN 259870-49-0 USPATFULL
CN 4,6-Quinazolinediamine, 2-(2-fluorophenyl)-N6-[(3-methoxyphenyl)methyl]-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



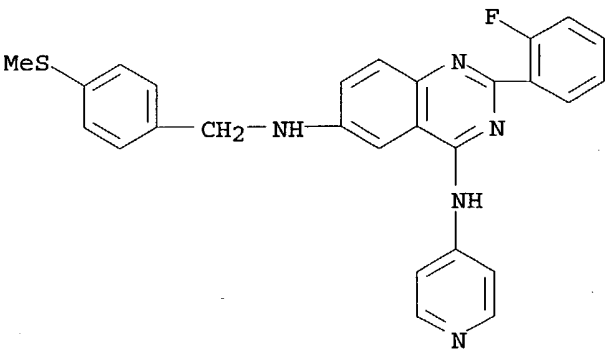
RN 259870-50-3 USPATFULL
CN 4,6-Quinazolinediamine, 2-(2-fluorophenyl)-N6-[(4-methoxyphenyl)methyl]-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



RN 259870-51-4 USPATFULL
CN 4,6-Quinazolinediamine, 2-(2-fluorophenyl)-N6-(2-methylpropyl)-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



RN 259870-52-5 USPATFULL
CN 4,6-Quinazolinediamine, 2-(2-fluorophenyl)-N6-[[4-(methylthio)phenyl]methyl]-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



L41 ANSWER 23 OF 37 USPATFULL on STN

ACCESSION NUMBER:	2001:136790 USPATFULL
TITLE:	Quinazoline derivatives as medicaments
INVENTOR(S):	Chakravarty, Sarvajit, Sunnyvale, CA, United States Dugar, Sundeep, Bridgewater, NJ, United States Perumattam, John J., Los Altos, CA, United States Schreiner, George F., Los Altos Hills, CA, United States Liu, David Y., Palo Alto, CA, United States Lewicki, John A., Los Gatos, CA, United States
PATENT ASSIGNEE(S):	Scios, Inc., Sunnyvale, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6277989	B1	20010821
APPLICATION INFO.:	US 2000-525034		20000314 (9)

RELATED APPLN. INFO.: Division of Ser. No. US 1999-383825, filed on 27 Aug 1999 Continuation-in-part of Ser. No. US 1998-141916, filed on 28 Aug 1998, now patented, Pat. No. US 6184226

DOCUMENT TYPE:	Utility
FILE SEGMENT:	GRANTED
PRIMARY EXAMINER:	Raymond, Richard L.
LEGAL REPRESENTATIVE:	Morrison & Foerster LLP
NUMBER OF CLAIMS:	6

EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 12 Drawing Figure(s); 10 Drawing Page(s)
LINE COUNT: 1181
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention is directed to methods to inhibit TGF-.beta. and/or **p38-.alpha. kinase** using compounds of the formula ##STR1##

or the pharmaceutically acceptable salts thereof

wherein R.sup.3 is a noninterfering substituent;

each Z is CR.sup.2 or N, wherein no more than two Z positions in ring A are N, and wherein two adjacent Z positions in ring A cannot be N;

each R.sup.2 is independently a noninterfering substituent;

L is a linker;

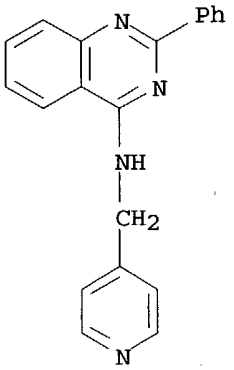
n is 0 or 1; and

Ar' is the residue of a cyclic aliphatic, cyclic heteroaliphatic, aromatic or heteroaromatic moiety optionally substituted with 1-3 noninterfering substituents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **165245-96-5**
(mediated disorders; treatment; prepn. of quinazolines as **p38-.alpha. kinase** and TGF-.beta. inhibitors)
RN 165245-96-5 USPATFULL
CN Kinase (phosphorylating), protein, RK (9CI) (CA INDEX NAME)

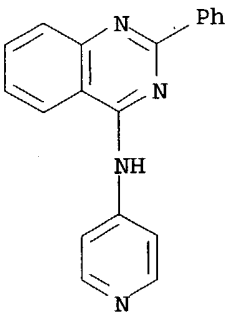
STRUCTURE DIAGRAM IS NOT AVAILABLE

IT **259870-32-1P 259870-33-2P 259870-34-3P**
259870-35-4P 259870-36-5P 259870-37-6P
259870-38-7P 259870-39-8P 259870-40-1P
259870-41-2P 259870-42-3P 259870-43-4P
259870-44-5P 259870-45-6P 259870-46-7P
259870-47-8P 259870-48-9P 259870-49-0P
259870-50-3P 259870-51-4P 259870-52-5P
(prepn. of quinazolines as **p38-.alpha. kinase** and TGF-.beta. inhibitors)
RN 259870-32-1 USPATFULL
CN 4-Quinazolinamine, 2-phenyl-N-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)

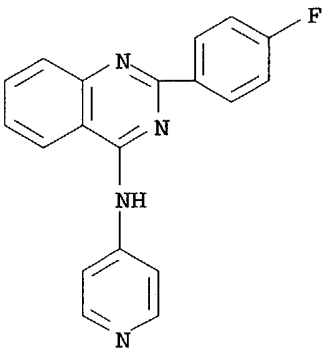


RN 259870-33-2 USPATFULL

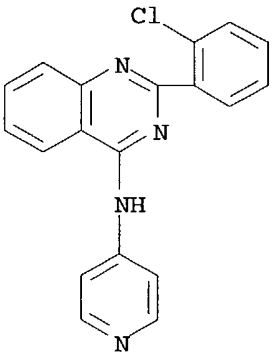
CN 4-Quinazolinamine, 2-phenyl-N-4-pyridinyl- (9CI) (CA INDEX NAME)



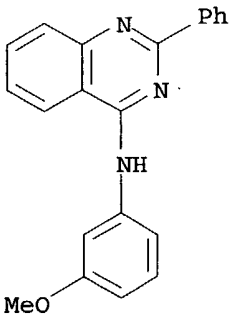
RN 259870-34-3 USPATFULL
CN 4-Quinazolinamine, 2-(4-fluorophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



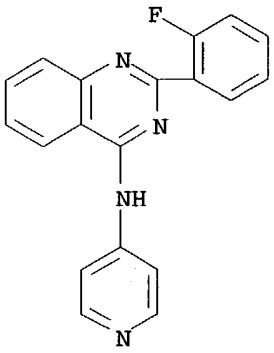
RN 259870-35-4 USPATFULL
CN 4-Quinazolinamine, 2-(2-chlorophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



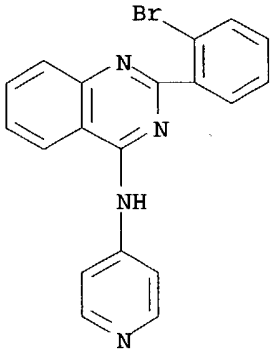
RN 259870-36-5 USPATFULL
CN 4-Quinazolinamine, N-(3-methoxyphenyl)-2-phenyl- (9CI) (CA INDEX NAME)



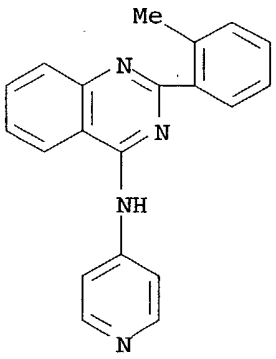
RN 259870-37-6 USPATFULL
CN 4-Quinazolinamine, 2-(2-fluorophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



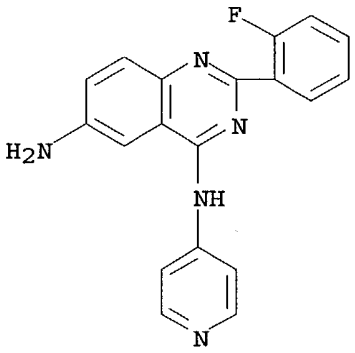
RN 259870-38-7 USPATFULL
CN 4-Quinazolinamine, 2-(2-bromophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



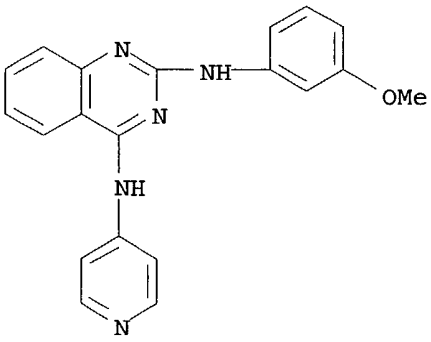
RN 259870-39-8 USPATFULL
CN 4-Quinazolinamine, 2-(2-methylphenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



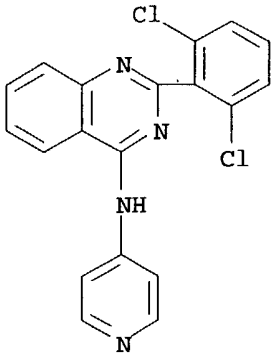
RN 259870-40-1 USPATFULL
CN 4,6-Quinazolinediamine, 2-(2-fluorophenyl)-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



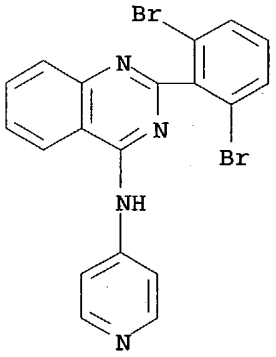
RN 259870-41-2 USPATFULL
CN 2,4-Quinazolinediamine, N2-(3-methoxyphenyl)-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



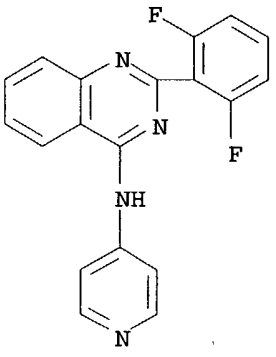
RN 259870-42-3 USPATFULL
CN 4-Quinazolinamine, 2-(2,6-dichlorophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



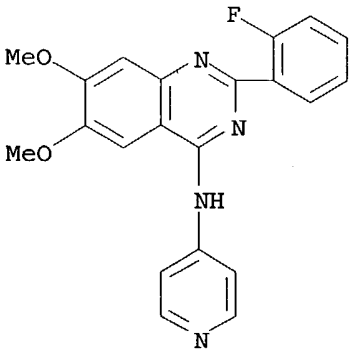
RN 259870-43-4 USPATFULL
CN 4-Quinazolinamine, 2-(2,6-dibromophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



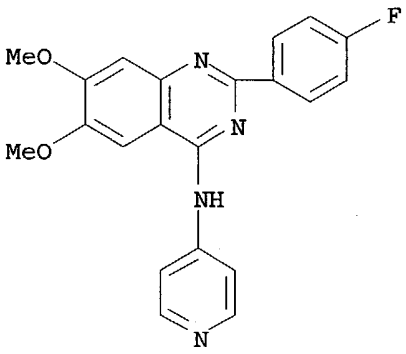
RN 259870-44-5 USPATFULL
CN 4-Quinazolinamine, 2-(2,6-difluorophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



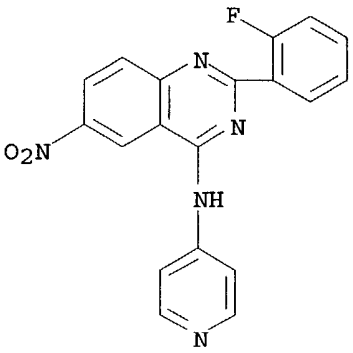
RN 259870-45-6 USPATFULL
CN 4-Quinazolinamine, 2-(2-fluorophenyl)-6,7-dimethoxy-N-4-pyridinyl- (9CI) (CA INDEX NAME)



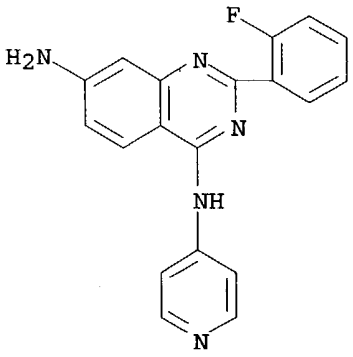
RN 259870-46-7 USPATFULL
CN 4-Quinazolinamine, 2-(4-fluorophenyl)-6,7-dimethoxy-N-4-pyridinyl- (9CI) (CA INDEX NAME)



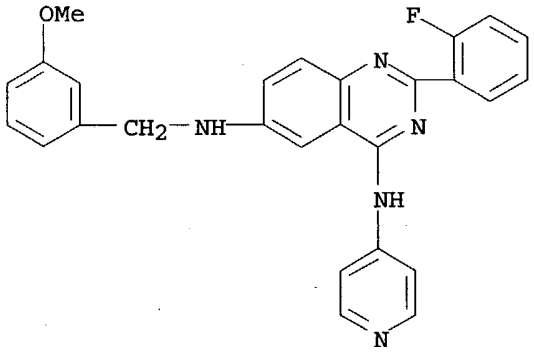
RN 259870-47-8 USPATFULL
CN 4-Quinazolinamine, 2-(2-fluorophenyl)-6-nitro-N-4-pyridinyl- (9CI) (CA INDEX NAME)



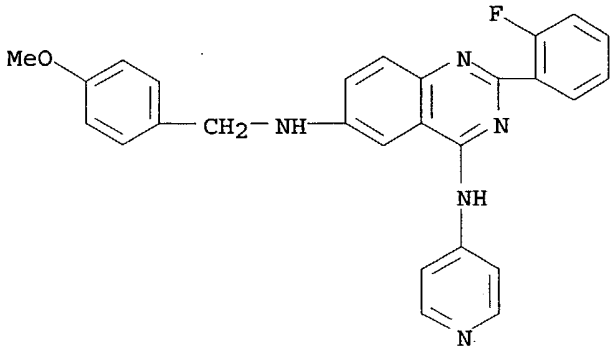
RN 259870-48-9 USPATFULL
CN 4,7-Quinazolinediamine, 2-(2-fluorophenyl)-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



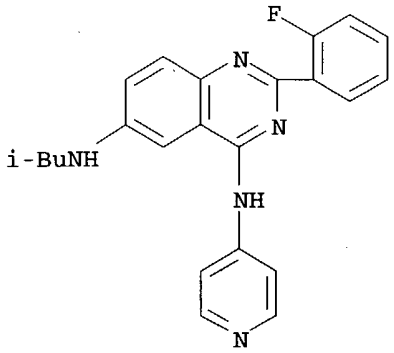
RN 259870-49-0 USPATFULL
CN 4,6-Quinazolinediamine, 2-(2-fluorophenyl)-N6-[(3-methoxyphenyl)methyl]-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



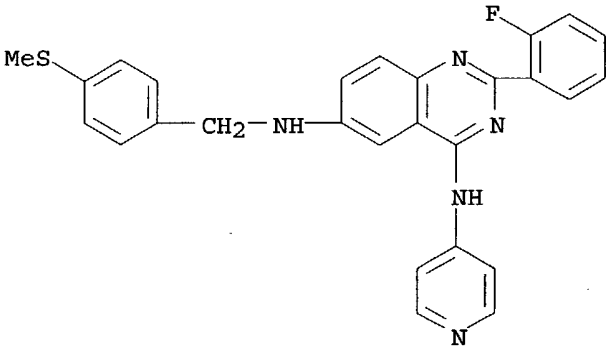
RN 259870-50-3 USPATFULL
CN 4,6-Quinazolinediamine, 2-(2-fluorophenyl)-N6-[(4-methoxyphenyl)methyl]-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



RN 259870-51-4 USPATFULL
CN 4,6-Quinazolinediamine, 2-(2-fluorophenyl)-N6-(2-methylpropyl)-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



RN 259870-52-5 USPATFULL
CN 4,6-Quinazolinediamine, 2-(2-fluorophenyl)-N6-[[4-(methylthio)phenyl]methyl]-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



L41 ANSWER 24 OF 37 USPATFULL on STN

ACCESSION NUMBER:	2001:18473 USPATFULL
TITLE:	Quinazoline derivatives as inhibitors of **P-38 .alpha.**
INVENTOR(S):	Chakravarty, Sarvajit, Sunnyvale, CA, United States Perumattam, John J., Los Altos, CA, United States Schreiner, George F., Los Altos Hills, CA, United States Liu, David Y., Palo Alto, CA, United States Lewicki, John A., Los Gatos, CA, United States
PATENT ASSIGNEE(S):	Scios Inc., Sunnyvale, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6184226	B1	20010206	
APPLICATION INFO.:	US 1998-141916		19980828	(9)
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Shah, Mukund J.			
ASSISTANT EXAMINER:	Truong, Tamthom N.			
LEGAL REPRESENTATIVE:	Morrison & Foerster LLP			
NUMBER OF CLAIMS:	17			
EXEMPLARY CLAIM:	1			
LINE COUNT:	785			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention describes compounds of the formula ##STR1##

and the pharmaceutically acceptable salts thereof

and the pharmaceutically acceptable salts thereof

wherein each R.sup.2 is independently a noninterfering substituent;

m is an integer of 0-4;

Z is CH or N;

R.sup.1 is H, alkyl (1-6C) or arylalkyl optionally substituted on the aryl group with 1-3 substituents independently selected from alkyl (1-6C), halo, OR, NR.sub.2, SR, --OOCR, --NROCR, RCO, --COOR, --CONR.sub.2, --SO.sub.2 NR.sub.2, CN, CF.sub.3, and NO.sub.2, wherein each R is independently H or lower alkyl (1-4C);

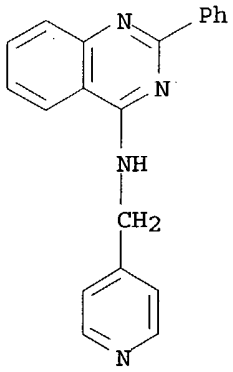
n is 0, 1 or 2;

Ar is phenyl, pyridyl, indolyl, or pyrimidyl, each optionally substituted with a group selected from the group consisting of optionally substituted alkyl (1-6C), halo, OR, NR.sub.2, SR, --OOCR, --NROCR, RCO, --COOR, --CONR.sub.2, SO.sub.2 NR.sub.2, CN, CF.sub.3, and NO.sub.2, wherein each R is independently H or lower alkyl (1-4C); and

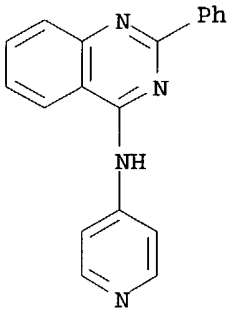
R.sup.3 is a branched or cyclic alkyl group (5-7C) or is phenyl optionally substituted with 1-2 substituents which substituents are selected from the group consisting of alkyl (1-6C), halo, OR, NR.sub.2, SR, --OOCR, --NROCR, RCO, --COOR, --CONR.sub.2, --SO.sub.2 NR.sub.2, CN, CF.sub.3, and NO.sub.2, wherein each R is independently H or lower alkyl (1-4C) which are useful as antiinflammatories and in treating cardiac disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **165245-96-5**
(mediated disorders; treatment; prepn. of quinazolines as **p38 -.alpha. kinase** and TGF-.beta. inhibitors)
RN 165245-96-5 USPATFULL
CN Kinase (phosphorylating), protein, RK (9CI) (CA INDEX NAME)

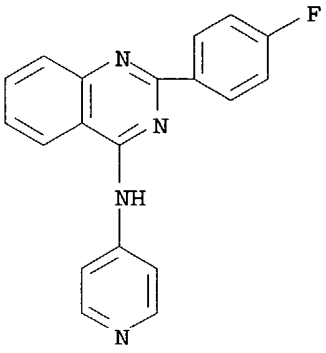
STRUCTURE DIAGRAM IS NOT AVAILABLE
IT **259870-32-1P 259870-33-2P 259870-34-3P**
259870-35-4P 259870-36-5P 259870-37-6P
259870-38-7P 259870-39-8P 259870-40-1P
259870-41-2P 259870-42-3P 259870-43-4P
259870-44-5P 259870-45-6P 259870-46-7P
259870-47-8P 259870-48-9P 259870-49-0P
259870-50-3P 259870-51-4P 259870-52-5P
(prepn. of quinazolines as **p38-.alpha. kinase** and TGF-.beta. inhibitors)
RN 259870-32-1 USPATFULL
CN 4-Quinazolinamine, 2-phenyl-N-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



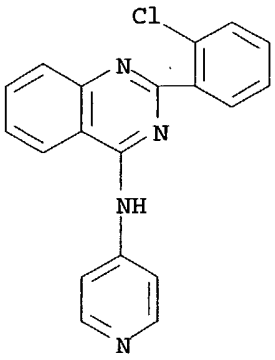
RN 259870-33-2 USPATFULL
CN 4-Quinazolinamine, 2-phenyl-N-4-pyridinyl- (9CI) (CA INDEX NAME)



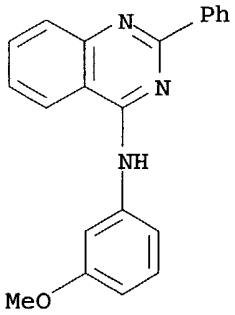
RN 259870-34-3 USPATFULL
CN 4-Quinazolinamine, 2-(4-fluorophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



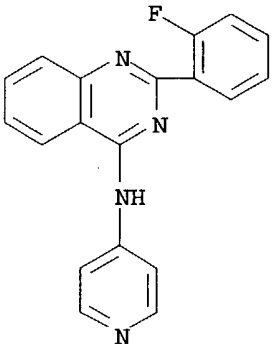
RN 259870-35-4 USPATFULL
CN 4-Quinazolinamine, 2-(2-chlorophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



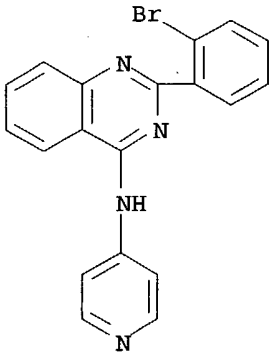
RN 259870-36-5 USPATFULL
CN 4-Quinazolinamine, N-(3-methoxyphenyl)-2-phenyl- (9CI) (CA INDEX NAME)



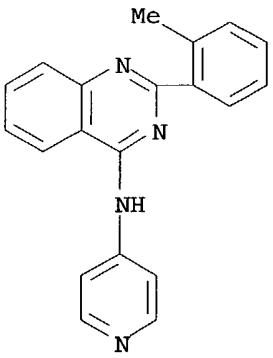
RN 259870-37-6 USPATFULL
CN 4-Quinazolinamine, 2-(2-fluorophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



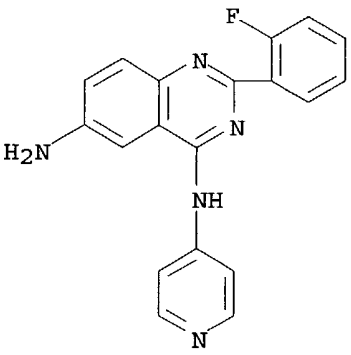
RN 259870-38-7 USPATFULL
CN 4-Quinazolinamine, 2-(2-bromophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



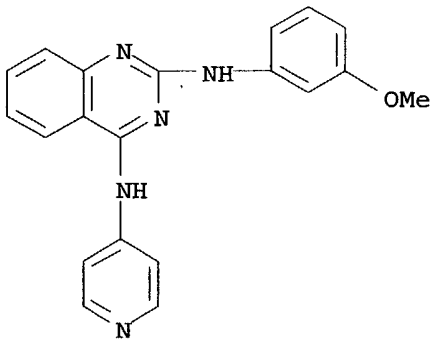
RN 259870-39-8 USPATFULL
CN 4-Quinazolinamine, 2-(2-methylphenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



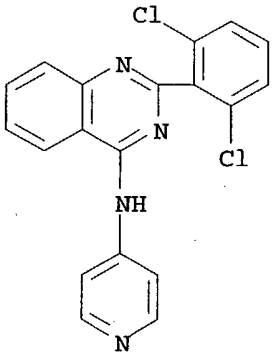
RN 259870-40-1 USPATFULL
CN 4,6-Quinazolinediamine, 2-(2-fluorophenyl)-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



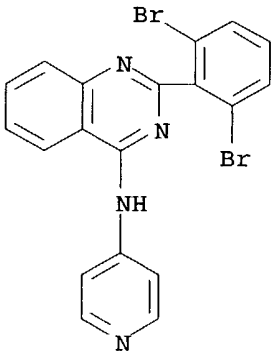
RN 259870-41-2 USPATFULL
CN 2,4-Quinazolinediamine, N2-(3-methoxyphenyl)-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



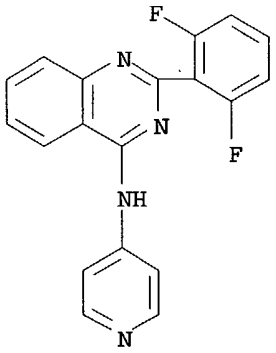
RN 259870-42-3 USPATFULL
CN 4-Quinazolinamine, 2-(2,6-dichlorophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



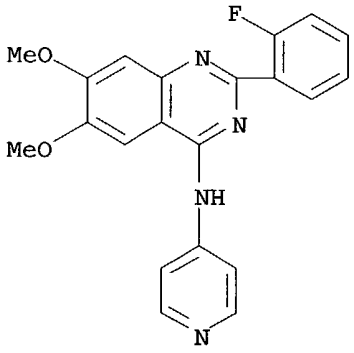
RN 259870-43-4 USPATFULL
CN 4-Quinazolinamine, 2-(2,6-dibromophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



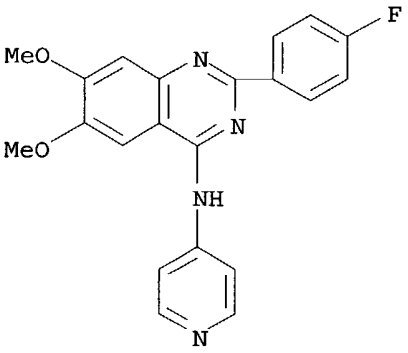
RN 259870-44-5 USPATFULL
CN 4-Quinazolinamine, 2-(2,6-difluorophenyl)-N-4-pyridinyl- (9CI) (CA INDEX NAME)



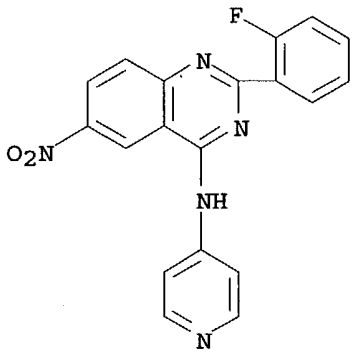
RN 259870-45-6 USPATFULL
CN 4-Quinazolinamine, 2-(2-fluorophenyl)-6,7-dimethoxy-N-4-pyridinyl- (9CI) (CA INDEX NAME)



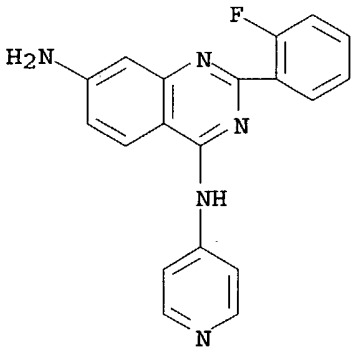
RN 259870-46-7 USPATFULL
CN 4-Quinazolinamine, 2-(4-fluorophenyl)-6,7-dimethoxy-N-4-pyridinyl- (9CI) (CA INDEX NAME)



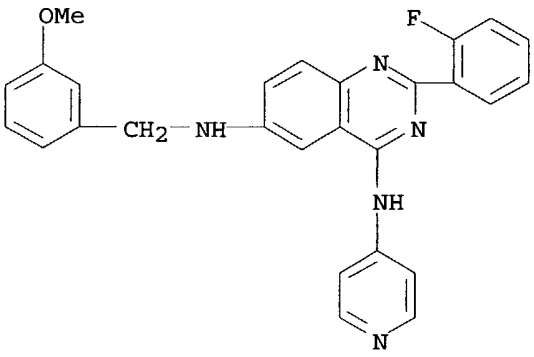
RN 259870-47-8 USPATFULL
CN 4-Quinazolinamine, 2-(2-fluorophenyl)-6-nitro-N-4-pyridinyl- (9CI) (CA INDEX NAME)



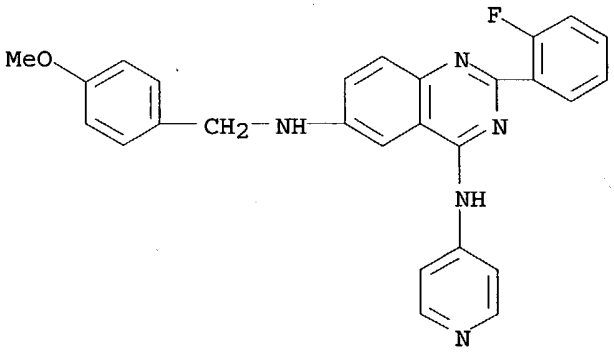
RN 259870-48-9 USPATFULL
CN 4,7-Quinazolinediamine, 2-(2-fluorophenyl)-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



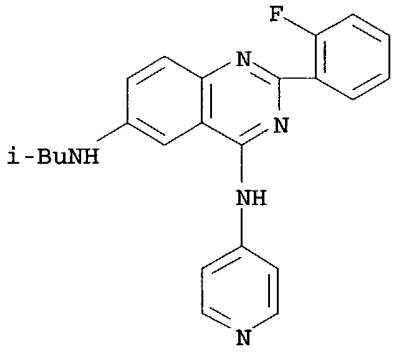
RN 259870-49-0 USPATFULL
CN 4,6-Quinazolinediamine, 2-(2-fluorophenyl)-N6-[(3-methoxyphenyl)methyl]-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



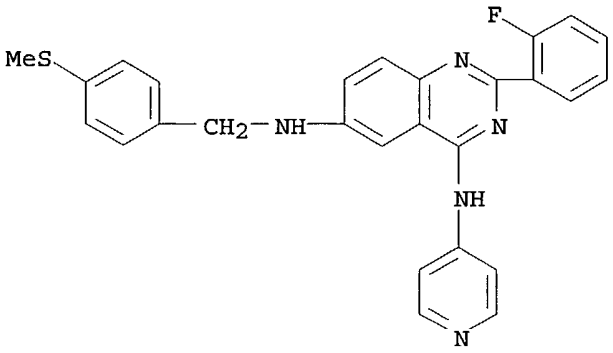
RN 259870-50-3 USPATFULL
CN 4,6-Quinazolinediamine, 2-(2-fluorophenyl)-N6-[(4-methoxyphenyl)methyl]-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



RN 259870-51-4 USPATFULL
CN 4,6-Quinazolinediamine, 2-(2-fluorophenyl)-N6-(2-methylpropyl)-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



RN 259870-52-5 USPATFULL
CN 4,6-Quinazolinediamine, 2-(2-fluorophenyl)-N6-[[4-(methylthio)phenyl]methyl]-N4-4-pyridinyl- (9CI) (CA INDEX NAME)



L41 ANSWER 25 OF 37 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2002136066 MEDLINE

DOCUMENT NUMBER: PubMed ID: 11827698
TITLE: Regulation of sarcolemmal Na(+)/H(+) exchange by hydrogen peroxide in adult rat ventricular myocytes.
AUTHOR: Snabaitis Andrew K; Hearse David J; Avkiran Metin
CORPORATE SOURCE: Centre for Cardiovascular Biology and Medicine, King's College London, The Rayne Institute, St. Thomas' Hospital, London SE1 7EH, UK.
SOURCE: Cardiovascular research, (2002 Feb 1) 53 (2) 470-80.
Journal code: 0077427. ISSN: 0008-6363.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200203
ENTRY DATE: Entered STN: 20020302
Last Updated on STN: 20021219
Entered Medline: 20020311

ABSTRACT:
OBJECTIVE: To characterise the effects of exogenous H(2)O(2) on sarcolemmal Na(+)/H(+) exchanger (NHE) activity and determine the roles of extracellular signal-regulated **kinase** (ERK), **p38** mitogen-activated protein **kinase** (**p38** MAPK) and protein **kinase** C (PKC) in observed effects. METHODS: Sarcolemmal H(+) efflux rate (J(H)) was determined by microepifluorescence at a pH(i) of 6.70 in adult rat ventricular myocytes, after two consecutive acid pulses in HCO(3)(-)-free medium; before the second pulse, cells (n=7-10/group) were exposed to H(2)O(2) or vehicle and the change in J(H) (DeltaJ(H)) was used to quantify the change in NHE activity. ERK and p38 MAPK activities were determined by immunoblotting with phosphospecific antibodies. RESULTS: Relative to control, DeltaJ(H) was increased by a 10-min exposure to 100, but not 1 or 10 microM H(2)O(2) (1000 microM was not tolerated); 3 or 6 min exposure to 100 microM H(2)O(2) was without effect. ERK and p38 MAPK activities were both increased by 100 microM H(2)O(2) (peak at 6 min); the ERK kinase inhibitor PD98059 (10 microM), but not the p38 MAPK inhibitor SB203580 (1 microM), inhibited the H(2)O(2)-induced increase in DeltaJ(H). H(2)O(2)-induced ERK activation was inhibited not only by PD98059 (10 microM), but also by the non-selective tyrosine kinase inhibitor genistein (3-100 microM), the EGF receptor kinase inhibitor AG1478 (3-300 nM) and the Src family kinase inhibitor PP2 (0.1-10 microM). The PKC inhibitors GF109203X (0.3-10 microM) and chelerythrine (1-30 microM) were without effect on ERK activation, although the former abolished the H(2)O(2)-induced increase in DeltaJ(H). CONCLUSIONS: Our data demonstrate that, in adult rat ventricular myocytes, (i) hydrogen peroxide stimulates sarcolemmal NHE activity, (ii) this response requires activation of ERK and PKC, but not p38 MAPK, (iii) ERK activation occurs through tyrosine kinase-mediated, but PKC-independent, mechanisms

CONTROLLED TERM: Check Tags: Male; Support, Non-U.S. Gov't
Animals
Cells, Cultured
DNA-Binding Proteins: PD, pharmacology
Enzyme Inhibitors: PD, pharmacology
Flavonoids: PD, pharmacology
Genistein: PD, pharmacology
*Hydrogen Peroxide: PD, pharmacology
Imidazoles: PD, pharmacology
Immunoblotting: MT, methods
Indoles: PD, pharmacology
Maleimides: PD, pharmacology
Mitogen-Activated Protein Kinases: AI, antagonists & inhibitors
Mitogen-Activated Protein Kinases: ME, metabolism
*Myocardium: ME, metabolism
Plant Proteins: PD, pharmacology

Protein Kinase C: ME, metabolism
Protein-Tyrosine Kinase: AI, antagonists & inhibitors
Pyridines: PD, pharmacology
Rats
Rats, Wistar
Receptor, Epidermal Growth Factor: AI, antagonists & inhibitors
*Sarcolemma: ME, metabolism
Signal Transduction: DE, drug effects
*Sodium-Hydrogen Antiporter: ME, metabolism
Tyrphostins: PD, pharmacology
src-Family Kinases: AI, antagonists & inhibitors

Structures for hit RNs from Medline & Embase printed at end of search

CAS REGISTRY NO.: 133052-90-1 (bisindolylmaleimide I); **170449-18-0 (tyrphostin AG 1478)**; 446-72-0 (Genistein); 7722-84-1 (Hydrogen Peroxide)

CHEMICAL NAME: 0 (DNA-Binding Proteins); 0 (Enzyme Inhibitors); 0 (Flavonoids); 0 (Imidazoles); 0 (Indoles); 0 (Maleimides); 0 (PD 98059); 0 (PP2 protein, Physcomitrella patens); 0 (Plant Proteins); 0 (Pyridines); 0 (SB 203580); 0 (Sodium-Hydrogen Antiporter); 0 (Tyrphostins); EC 2.7.1.112 (Protein-Tyrosine Kinase); EC 2.7.1.112 (Receptor, Epidermal Growth Factor); EC 2.7.1.112 (src-Family Kinases); EC 2.7.1.37 (Mitogen-Activated Protein Kinases); EC 2.7.1.37 (Protein Kinase C); EC 2.7.10.- (mitogen-activated protein **kinase p38**)

L41 ANSWER 26 OF 37 MEDLINE on STN
ACCESSION NUMBER: 2003089457 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12601051
TITLE: P2Y receptor-mediated stimulation of Muller glial cell DNA synthesis: dependence on EGF and PDGF receptor transactivation.
AUTHOR: Milenkovic Ivan; Weick Michael; Wiedemann Peter; Reichenbach Andreas; Bringmann Andreas
CORPORATE SOURCE: Department of Neurophysiology, Paul Flechsig Institute of Brain Research, Leipzig, Germany.
SOURCE: Investigative ophthalmology & visual science, (2003 Mar) 44 (3) 1211-20.
Journal code: 7703701. ISSN: 0146-0404.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 20030226
Last Updated on STN: 20030311
Entered Medline: 20030310

ABSTRACT:
PURPOSE: To determine whether P2Y receptor-evoked proliferation of Muller glial cells depends on transactivation of receptor tyrosine kinases. METHODS: Primary cultures of Muller cells of the guinea pig were treated with test substances for 16 hours. The DNA synthesis rate was assessed by a bromodeoxyuridine (BrdU) immunoassay, and the phosphorylation states of the extracellular signal-regulated kinase (ERK1/2) and the **p38** mitogen-activated protein **kinase** (**p38** MAPK) were determined by Western blot analysis. RESULTS: In Muller cells, the mitogenic effect of P2Y receptor activation by extracellular adenosine triphosphate (ATP) depended on transactivation of both the platelet-derived growth factor (PDGF) and the epidermal growth factor (EGF) receptor tyrosine kinases, as suggested by the blocking effects of the tyrphostins AG1296 and AG1478 on the ATP-induced proliferation and phosphorylation of ERK1/2. Moreover, the PDGF-induced proliferation may depend on transactivation of the EGF receptor kinase.

Antibodies against heparin-binding EGF (HB-EGF) or PDGF, as well as inhibition of matrix metalloproteinases (MMPs) blocked ATP-evoked proliferation. At least one metalloproteinase (MMP-9), was implicated in the signal transfer from P2Y to EGF receptors. In contrast, the mitogenic effect of fetal calf serum was independent of growth factor receptor activity. P2Y receptor activation stimulated Muller cell proliferation by activating the ERK1/2 and the phosphatidylinositol 3 (PI3) kinase signaling pathways, whereas the p38 MAPK pathway was not involved in mitogenic signaling. CONCLUSIONS: The present data suggest that P2Y-receptor-induced mitogenic signaling in Muller cells is mediated by transactivation of the PDGF and EGF receptor tyrosine kinases. The transactivation may be mediated by release of PDGF and MMP-dependent shedding of HB-EGF from the Muller cell matrix, respectively. The transactivation of the receptor tyrosine kinases may result in activation of ERK1/2 and PI3 kinase and an increase in the proliferation rate.

CONTROLLED TERM: Check Tags: Comparative Study; Support, Non-U.S. Gov't
*Adenosine Triphosphate: PD, pharmacology
Animals
Blotting, Western
Calcium: ME, metabolism
Cell Division
Cells, Cultured
*DNA: BI, biosynthesis
DNA Replication
Epidermal Growth Factor: PD, pharmacology
Guinea Pigs
Matrix Metalloproteinases: AI, antagonists & inhibitors
Mitogen-Activated Protein Kinases: AI, antagonists & inhibitors
Mitogen-Activated Protein Kinases: ME, metabolism
*Neuroglia: DE, drug effects
Neuroglia: ME, metabolism
Phosphorylation
Platelet-Derived Growth Factor: PD, pharmacology
Receptor, Epidermal Growth Factor: AI, antagonists & inhibitors
*Receptor, Epidermal Growth Factor: ME, metabolism
Receptors, Platelet-Derived Growth Factor: AI, antagonists & inhibitors
*Receptors, Platelet-Derived Growth Factor: ME, metabolism
*Receptors, Purinergic P2: ME, metabolism
Tyrphostins: PD, pharmacology
p42 MAP Kinase: AI, antagonists & inhibitors
p42 MAP Kinase: ME, metabolism

CAS REGISTRY NO.: 146535-11-7 (tyrphostin AG 1296); **170449-18-0 (tyrphostin AG 1478)**; 56-65-5 (Adenosine Triphosphate); 62229-50-9 (Epidermal Growth Factor); 7440-70-2 (Calcium); 9007-49-2 (DNA)

CHEMICAL NAME: 0 (Platelet-Derived Growth Factor); 0 (Receptors, Purinergic P2); 0 (Tyrphostins); EC 2.7.1.112 (Receptor, Epidermal Growth Factor); EC 2.7.1.112 (Receptors, Platelet-Derived Growth Factor); EC 2.7.1.37 (Mitogen-Activated Protein Kinases); EC 2.7.1.37 (p42 MAP Kinase); EC 2.7.10.- (mitogen-activated protein kinase 3); EC 2.7.10.- (mitogen-activated protein **kinase p38**); EC 3.4.24.- (Matrix Metalloproteinases)

L41 ANSWER 27 OF 37 MEDLINE on STN
ACCESSION NUMBER: 2002682434 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12444032
TITLE: Oxidative stress induces arachidonate release from human lung cells through the epithelial growth factor receptor pathway.

AUTHOR: Pawliczak Rafal; Huang Xiu-Li; Nanavaty Uday B; Lawrence Marion; Madara Patricia; Shelhamer James H
CORPORATE SOURCE: Critical Care Medicine Department, Warren Grant Magnuson Clinical Center, National Institutes of Health, Bethesda, Maryland 20892, USA.
SOURCE: American journal of respiratory cell and molecular biology, (2002 Dec) 27 (6) 722-31.
Journal code: 8917225. ISSN: 1044-1549.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200301
ENTRY DATE: Entered STN: 20021122
Last Updated on STN: 20030109
Entered Medline: 20030108

ABSTRACT:
Oxidative stress is thought to be a factor influencing many inflammatory responses, including arachidonic acid (AA) release. We have studied the effect of hydrogen peroxide on AA and prostaglandin E(2) release, cytosolic phospholipase (cPLA(2)) steady-state mRNA, cPLA(2) protein levels, cPLA(2) enzyme activity, and cPLA(2) phosphorylation in a human lung epithelial cell line: A549 cells. Hydrogen peroxide caused a dose-dependent increase of A23187-stimulated AA and prostaglandin E(2) release, with a maximum effect at 1 h. This effect is associated with a maximum specific cPLA(2) activity at 1 h, and with a significant increase in cPLA(2) Serine 505 phosphorylation. All these effects were abolished, in a dose-related manner, by the epithelial growth factor receptor kinase inhibitor, AG 1478. To further investigate the pathway leading to the increase cPLA(2) phosphorylation, we used cells transfected with a Ras dominant negative vector and mitogen-activated protein kinase/extracellular signal-regulated **kinase** (MEK) and **p38** ***kinase*** inhibitors. Cells transfected with the Ras dominant negative vector exhibited diminished hydrogen peroxide-induced AA release and cPLA(2) phosphorylation as compared with cells transfected with the Ras expression vector. Both MEK and **p38** **kinase** inhibitors inhibited the hydrogen peroxide effect on AA release and specific cPLA(2) activity. Finally, cells stably transfected with an antisense cPLA(2) vector exhibited diminished A23187-stimulated AA release in response to hydrogen peroxide as compared with cells stably transfected with empty expression vector. Collectively, these data show that hydrogen peroxide increases cPLA(2) activity through its phosphorylation utilizing an epithelial growth factor/Ras/extracellular signal-regulated **kinase** and **p38** pathway.

CONTROLLED TERM: Check Tags: Human
Antineoplastic Agents: PD, pharmacology
*Arachidonic Acid: ME, metabolism
Calcium: ME, metabolism
Cells, Cultured
Cytosol: EN, enzymology
Enzyme Inhibitors: PD, pharmacology
Flavonoids: PD, pharmacology
Hydrogen Peroxide: PD, pharmacology
Imidazoles: PD, pharmacology
Ionophores: PD, pharmacology
Lung: CY, cytology
*Lung: ME, metabolism
Mitogen-Activated Protein Kinases: AI, antagonists & inhibitors
Mitogen-Activated Protein Kinases: ME, metabolism
Oxidants: PD, pharmacology
Oxidative Stress: DE, drug effects
*Oxidative Stress: PH, physiology
Phospholipases A: GE, genetics

Phospholipases A: ME, metabolism
Phosphorylation: DE, drug effects
Platelet Activating Factor: PD, pharmacology
Protein-Serine-Threonine Kinases: AI, antagonists & inhibitors
Protein-Serine-Threonine Kinases: ME, metabolism
Pyridines: PD, pharmacology
RNA, Messenger: AN, analysis
*Receptor, Epidermal Growth Factor: ME, metabolism
Tumor Necrosis Factor: PD, pharmacology
Tyrosine: ME, metabolism
Tyrphostins: PD, pharmacology
p42 MAP Kinase: ME, metabolism
ras Proteins: GE, genetics
ras Proteins: ME, metabolism

CAS REGISTRY NO.: **170449-18-0 (tyrphostin AG 1478)**; 506-32-1 (Arachidonic Acid); 55520-40-6 (Tyrosine); 7440-70-2 (Calcium); 7722-84-1 (Hydrogen Peroxide)

CHEMICAL NAME: 0 (Antineoplastic Agents); 0 (Enzyme Inhibitors); 0 (Flavonoids); 0 (Imidazoles); 0 (Ionophores); 0 (Oxidants); 0 (PD 98059); 0 (Platelet Activating Factor); 0 (Pyridines); 0 (RNA, Messenger); 0 (SB 203580); 0 (Tumor Necrosis Factor); 0 (Tyrphostins); EC 2.7.1.- (mitogen activated protein kinase kinase kinase 1); EC 2.7.1.112 (Receptor, Epidermal Growth Factor); EC 2.7.1.37 (Mitogen-Activated Protein Kinases); EC 2.7.1.37 (Protein-Serine-Threonine Kinases); EC 2.7.1.37 (p42 MAP Kinase); EC 2.7.10.- (mitogen-activated protein kinase 3); EC 2.7.10.- (mitogen-activated protein **kinase p38**); EC 3.1.1.- (Phospholipases A); EC 3.6.1.- (ras Proteins)

L41 ANSWER 28 OF 37 MEDLINE on STN
ACCESSION NUMBER: 2001219101 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11309236
TITLE: Thrombin-induced **p38** mitogen-activated protein **kinase** activation is mediated by epidermal growth factor receptor transactivation pathway.
AUTHOR: Kanda Y; Mizuno K; Kuroki Y; Watanabe Y
CORPORATE SOURCE: Department of Pharmacology, National Defense Medical College, 3-2, Namiki, Tokorozawa, Saitama, 359-8513, Japan.. kanda@cc.ndmc.ac.jp
SOURCE: British journal of pharmacology, (2001 Apr) 132 (8) 1657-64.
Journal code: 7502536. ISSN: 0007-1188.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010723
Last Updated on STN: 20010723
Entered Medline: 20010719

ABSTRACT:
Thrombin is a potent mitogen for vascular smooth muscle cells (VSMC) and has been implicated its pathogenic role in vascular remodelling. However, the signalling pathways by which thrombin mediates its mitogenic response are not fully understood. We have previously reported that thrombin activates ***p38*** mitogen-activated protein **kinase** (**p38** MAPK) by a tyrosine kinase-dependent mechanism, and that p38 MAPK has a role in thrombin-induced mitogenic response in rat VSMC. In the present study, we examine the involvement of epidermal growth factor (EGF) receptor in

thrombin-induced p38 MAPK activation. We found that thrombin induced EGF receptor tyrosine phosphorylation (transactivation) in A10 cells, a clonal VSMC cell line. A selective inhibitor of EGF receptor **kinase** (AG1478) inhibited the **p38** MAPK activation in a dose-dependent manner, whereas it had no effect on the response to platelet-derived growth factor (PDGF). EGF receptor phosphorylation induced by thrombin was inhibited by BAPTA-AM and GF109203X, which suggest a requirement for intracellular Ca(2+) increase and protein kinase C. We next examined the effect of AG1478 on thrombin-induced DNA synthesis. AG1478 inhibited thrombin-induced DNA synthesis in a dose-dependent manner. In contrast, PDGF-induced DNA synthesis was not affected by AG1478. In conclusion, these data suggest that the EGF receptor transactivation and subsequent p38 MAPK activation is required for thrombin-induced proliferation of VSMC.

CONTROLLED TERM: Check Tags: Human; Support, Non-U.S. Gov't
Blotting, Western
Calcium: ME, metabolism
Cells, Cultured
DNA: BI, biosynthesis
Enzyme Activation: DE, drug effects
Enzyme Inhibitors: PD, pharmacology
GTP-Binding Proteins: ME, metabolism
Mitogen-Activated Protein Kinases: AI, antagonists & inhibitors
*Mitogen-Activated Protein Kinases: ME, metabolism
Muscle, Smooth, Vascular: CY, cytology
Muscle, Smooth, Vascular: DE, drug effects
Phosphorylation
Precipitin Tests
Receptor, Epidermal Growth Factor: DE, drug effects
*Receptor, Epidermal Growth Factor: PH, physiology
Signal Transduction: DE, drug effects
*Signal Transduction: PH, physiology
*Thrombin: PD, pharmacology
Trans-Activation (Genetics): DE, drug effects
*Trans-Activation (Genetics): PH, physiology
Tyrphostins: PD, pharmacology
Virulence Factors, Bordetella: PD, pharmacology

CAS REGISTRY NO.: **170449-18-0 (tyrphostin AG 1478)**; 7440-70-2 (Calcium); 9007-49-2 (DNA)

CHEMICAL NAME: 0 (Enzyme Inhibitors); 0 (Tyrphostins); 0 (Virulence Factors, Bordetella); EC 2.7.1.112 (Receptor, Epidermal Growth Factor); EC 2.7.1.37 (Mitogen-Activated Protein Kinases); EC 2.7.10.- (JNK mitogen-activated protein kinases); EC 2.7.10.- (mitogen-activated protein **kinase p38**); EC 3.4.21.5 (Thrombin); EC 3.6.1.- (GTP-Binding Proteins)

L41 ANSWER 29 OF 37 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2004135966 EMBASE

TITLE: Recent kinase and kinase inhibitor x-ray structures: Mechanisms of inhibition and selectivity insights.

AUTHOR: Cherry M.; Williams D.H.

CORPORATE SOURCE: D.H. Williams, Sareum Ltd., 61 Cow Lane, Cambridge CB1 5HB, United Kingdom. david.williams@sareum.co.uk

SOURCE: Current Medicinal Chemistry, (2004) 11/6 (663-673). Refs: 50
ISSN: 0929-8673 CODEN: CMCHE7

COUNTRY: Netherlands

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
016 Cancer

029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index

LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT:
Recent years have seen an explosion in the number of publicly available x-ray crystal structures of protein kinases. These structures have provided a wealth of information on the regulatory mechanisms, conformational plasticity and drugability of this important family of enzymes. Drawing upon structural information, new insights into the development of protein kinase inhibitors are discussed including de-novo design, molecular templates for ATP competitive inhibitors and alternative mechanisms of inhibition. The highly conserved nature of the ATP binding site is of central concern to drug development and the concept of a selectivity profile has arisen with structure-based design emerging as a key tool for addressing the challenges of specificity. In addition, protein-ligand complexes, where the enzyme is in an inactive conformation, signify an alternate approach to protein kinase inhibition. The belief that an inactive kinase presents a less conserved target is reviewed using observations on the structural changes occurring during protein kinase regulation. .COPYRGT. Bentham Science Publishers Ltd.

CONTROLLED TERM: Medical Descriptors:
X ray crystallography
crystal structure
drug structure
structure activity relation
structure analysis
enzyme inhibition
enzyme mechanism
enzyme structure
drug selectivity
drug conformation
drug design
competitive inhibition
drug binding site
drug specificity
protein lipid interaction
drug targeting
enzyme regulation
enzyme activity
drug receptor binding
breast cancer: DT, drug therapy
lung cancer: DT, drug therapy
lung non small cell cancer: DT, drug therapy
human
clinical trial
review
Drug Descriptors:
***protein tyrosine kinase inhibitor: CT, clinical trial**
***protein tyrosine kinase inhibitor: AN, drug analysis**
***protein tyrosine kinase inhibitor: CM, drug comparison**
***protein tyrosine kinase inhibitor: DV, drug development**
***protein tyrosine kinase inhibitor: DT, drug therapy**
***protein tyrosine kinase inhibitor: PD, pharmacology**
adenosine triphosphate: EC, endogenous compound

cyclin dependent kinase 2: EC, endogenous compound
cyclin dependent kinase 5: EC, endogenous compound
cyclin dependent kinase 6: EC, endogenous compound
protein kinase B: EC, endogenous compound
mitogen activated protein kinase: EC, endogenous compound
stress activated protein kinase: EC, endogenous compound
mitogen activated protein kinase p38: EC, endogenous compound
connectin: EC, endogenous compound
transforming growth factor beta: EC, endogenous compound
casein kinase: EC, endogenous compound
death associated protein kinase: EC, endogenous compound
Abelson kinase: EC, endogenous compound
Bruton tyrosine kinase: EC, endogenous compound
casein kinase I: EC, endogenous compound
epidermal growth factor receptor kinase: EC, endogenous compound
angiopoietin receptor: EC, endogenous compound
fibroblast growth factor: EC, endogenous compound
somatomedin receptor: EC, endogenous compound
oxindole: AN, drug analysis
oxindole: DV, drug development
oxindole: PD, pharmacology
mitogen activated protein kinase inhibitor: AN, drug analysis
mitogen activated protein kinase inhibitor: CM, drug comparison
mitogen activated protein kinase inhibitor: DV, drug development
mitogen activated protein kinase inhibitor: PD, pharmacology
cyclin dependent kinase inhibitor: CT, clinical trial
cyclin dependent kinase inhibitor: AN, drug analysis
cyclin dependent kinase inhibitor: CM, drug comparison
cyclin dependent kinase inhibitor: DV, drug development
cyclin dependent kinase inhibitor: DT, drug therapy
cyclin dependent kinase inhibitor: PD, pharmacology
purvalanol: CM, drug comparison
purvalanol: PD, pharmacology
olomoucine: CM, drug comparison
olomoucine: PD, pharmacology
imatinib: AN, drug analysis
imatinib: CM, drug comparison
imatinib: DV, drug development
imatinib: PD, pharmacology
roscovitine: CT, clinical trial
roscovitine: DT, drug therapy
roscovitine: PD, pharmacology
gefitinib: CT, clinical trial
gefitinib: DT, drug therapy
gefitinib: PD, pharmacology
vatalanib: CT, clinical trial
vatalanib: DT, drug therapy
vatalanib: PD, pharmacology
unindexed drug

CAS REGISTRY NO.: (adenosine triphosphate) 15237-44-2, 56-65-5, 987-65-5; (cyclin dependent kinase 2) 141349-86-2; (protein kinase B) 148640-14-6; (mitogen activated protein kinase) 142243-02-5; (stress activated protein kinase) 155215-87-5; (casein kinase) 52660-18-1; (death associated protein kinase) 169150-71-4; (Bruton tyrosine kinase) 149147-12-6; (epidermal growth factor receptor kinase) 79079-06-4;

(fibroblast growth factor) 62031-54-3; (oxindole) 59-48-3; (olomoucine) 101622-51-9; (imatinib) 152459-95-5, 220127-57-1; (roscovitine) 186692-46-6; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (vatalanib) 212141-54-3, 212142-18-2

CHEMICAL NAME: (1) Iressa; (2) Ptk 787; (3) Vatalanib; Gleevec
COMPANY NAME: (1) Astra Zeneca; (3) Novartis; Cyclacel

L41 ANSWER 30 OF 37 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2004219466 EMBASE
TITLE: Evaluation of kinase inhibitor selectivity by chemical proteomics.
AUTHOR: Daub H.; Godl K.; Brehmer D.; Klebl B.; Muller G.
CORPORATE SOURCE: H. Daub, Axxima Pharmaceuticals AG, Max-Lebsche-Platz 32, 81377 Munchen, Germany. henrik.daub@axxima.com
SOURCE: Assay and Drug Development Technologies, (2004) 2/2 (215-224).
Refs: 35
ISSN: 1540-658X CODEN: ADDTAR
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:

Small-molecule inhibitors of protein kinases constitute a novel class of drugs for therapeutic intervention in a variety of human diseases. Most of these agents target the relatively conserved ATP-binding site of protein kinases and have only been tested against a rather small subset of all human protein kinases. Therefore, the selectivity of protein kinase inhibitors has remained a widely underestimated, but highly important issue in drug development programs. In this review, we focus on the recent advancement of chemical proteomic methods to evaluate drug selectivity in an unbiased, comprehensive way. Efficient affinity purification procedures using immobilized kinase inhibitors combined with the sensitivity of mass spectrometry detection permit the mapping of drug targets on a proteome-wide scale. Data from this type of assessment can be used to set up tailor-made selectivity panels, which guide compound development in the context of the most relevant off-targets during lead optimization. In cases in which identified alternative targets are of validated clinical relevance, chemical proteomics provides the opportunity to repeatedly exploit a once established kinase inhibitor principle for additional target kinases and can thereby dramatically shorten the time toward highly selective, preclinical candidates. Moreover, the identification of alternative targets for preclinical or clinical drugs can provide new insights into their cellular modes of action, which might help to define those disease settings in which the most beneficial therapeutic effect is likely to occur. .COPYRGT. Mary Ann Liebert, Inc.

CONTROLLED TERM: Medical Descriptors:
*proteomics
drug screening
drug selectivity
molecular size
drug classification
drug indication
drug targeting
genetic conservation
binding site
drug research

analytic method
binding affinity
enzyme purification
electrophoretic mobility
sensitivity analysis
mass spectrometry
peptide mapping
validation process
time
drug mechanism
treatment outcome
drug efficacy
drug structure
human
nonhuman
clinical trial
review
Drug Descriptors:
*protein kinase inhibitor: CT, clinical trial
*protein kinase inhibitor: AN, drug analysis
*protein kinase inhibitor: DV, drug development
*protein kinase inhibitor: PD, pharmacology
adenosine triphosphate: EC, endogenous compound
protein kinase: EC, endogenous compound
proteome: EC, endogenous compound
protein tyrosine kinase inhibitor: CT, clinical trial
protein tyrosine kinase inhibitor: AN, drug analysis
protein tyrosine kinase inhibitor: PD, pharmacology
imatinib: AN, drug analysis
imatinib: PD, pharmacology
gefitinib: AN, drug analysis
gefitinib: PD, pharmacology
quinazoline derivative: AN, drug analysis
quinazoline derivative: PD, pharmacology
erlotinib: AN, drug analysis
erlotinib: PD, pharmacology
epidermal growth factor: EC, endogenous compound
antineoplastic agent: CT, clinical trial
antineoplastic agent: AN, drug analysis
antineoplastic agent: PD, pharmacology
cyclin dependent kinase inhibitor: CT, clinical trial
cyclin dependent kinase inhibitor: AN, drug analysis
cyclin dependent kinase inhibitor: PD, pharmacology
pha 539136: AN, drug analysis
pha 539136: CM, drug comparison
pha 539136: PD, pharmacology
flavopiridol: CT, clinical trial
flavopiridol: AN, drug analysis
flavopiridol: PD, pharmacology
mitogen activated protein kinase p38: EC, endogenous compound
mitogen activated protein kinase inhibitor: CT, clinical trial
mitogen activated protein kinase inhibitor: AN, drug analysis
mitogen activated protein kinase inhibitor: PD, pharmacology
pi 51: AN, drug analysis
pi 51: CM, drug comparison
pi 51: PD, pharmacology

antirheumatic agent: CT, clinical trial
antirheumatic agent: AN, drug analysis
antirheumatic agent: PD, pharmacology
sb 242234: CT, clinical trial
sb 242234: AN, drug analysis
sb 242234: CM, drug comparison
sb 242234: PD, pharmacology
birb 796: CT, clinical trial
birb 796: AN, drug analysis
birb 796: CM, drug comparison
birb 796: PD, pharmacology
methotrexate
purvalanol B: AN, drug analysis
purvalanol B: PD, pharmacology
mitogen activated protein kinase: EC, endogenous compound
glycogen synthase kinase 3
n (2 aminoethyl) 5 isoquinolinesulfonamide: AN, drug analysis
n (2 aminoethyl) 5 isoquinolinesulfonamide: PD, pharmacology
cyclin dependent kinase 2
pyrrolopyrimidine derivative: AN, drug analysis
pyrrolopyrimidine derivative: PD, pharmacology
tws 119: AN, drug analysis
tws 119: CM, drug comparison
tws 119: PD, pharmacology
4 (4 fluorophenyl) 2 (4 methylsulfinylphenyl) 5 (4 pyridyl)imidazole: PD, pharmacology
unindexed drug
unclassified drug
sb 242235

CAS REGISTRY NO.: (adenosine triphosphate) 15237-44-2, 56-65-5, 987-65-5; (protein kinase) 9026-43-1; (imatinib) 152459-95-5, 220127-57-1; (gefitinib) **184475-35-2, 184475-55-6, 184475-56-7**; (erlotinib) **183319-69-9, 183321-74-6**; (epidermal growth factor) 62229-50-9; (flavopiridol) 146426-40-6; (methotrexate) 15475-56-6, 59-05-2, 7413-34-5; (purvalanol B) 212844-54-7; (mitogen activated protein kinase) 142243-02-5; (n (2 aminoethyl) 5 isoquinolinesulfonamide) 84468-17-7; (cyclin dependent kinase 2) 141349-86-2; (4 (4 fluorophenyl) 2 (4 methylsulfinylphenyl) 5 (4 pyridyl)imidazole) 152121-47-6

CHEMICAL NAME: (1) Sti 571; (2) Gleevec; (3) Zd 1839; (4) Iressa; (5) Osi 774; (6) Tarceva; Sb 242235; Birb 796; H 9; Pha 539136; Tws 119; Sb 203580; Pi 51

COMPANY NAME: (2) Novartis; (4) Astra Zeneca; (6) Osi

L41 ANSWER 31 OF 37 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2003216391 EMBASE

TITLE: Activation of epidermal growth factor receptor is responsible for pervanadate-induced phospholipase D activation.

AUTHOR: Kim Y.-R.; Cha H.-Y.; Lim K.; Hwang B.-D.; Hoe K.-L.; Namgung U.; Park S.-K.

CORPORATE SOURCE: S.-K. Park, Department of Biochemistry, College of Medicine, Chungnam National University, Daejeon 301-130, Korea, Republic of. parksk@cnu.ac.kr

SOURCE: Experimental and Molecular Medicine, (30 Apr 2003) 35/2 (118-124).
Refs: 31

ISSN: 1226-3613 CODEN: EMMEF3
COUNTRY: Korea, Republic of
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
Pervanadate, a complex of vanadate and H(2)O(2), has an insulin mimetic effect, and acts as an inhibitor of protein tyrosine phosphatase. Pervanadate-induced phospholipase D (PLD) activation is known to be dependent on the tyrosine phosphorylation of cellular proteins and protein kinase C (PKC) activation, and yet underlying molecular mechanisms are not clearly understood. Here, we investigated the signaling pathway of pervanadate-induced PLD activation in Rat2 fibroblasts. Pervanadate increased PLD activity in dose- and time-dependent manner. Protein tyrosine kinase inhibitor, genistein, blocked PLD activation. Interestingly, AG-1478, a specific inhibitor of the tyrosine kinase activity of epidermal growth factor receptor (EGFR) blocked not only the PLD activation completely but also phosphorylation of **p38** mitogenactivated protein **kinase** (MAPK). However, AG-1295, an inhibitor specific for the tyrosine kinase activity of pletlet drived growth factor receptor (PDGFR) did not show any effect on the PLD activation by pervanadate. We further found that pervanadate increased phosphorylation levels of **p38**, extracellular signal-regulated **kinase** (ERK) and c-Jun NH(2)-terminal **kinase** (JNK). SB203580, a **p38** MAPK inhibitor, blocked the PLD activation completely. However, the inhibitions of ERK by the treatment of PD98059 or of JNK by the overexpression of JNK interacting peptide JBD did not show any effect on pervanadate-induced PLD activation. Inhibition or down-regulation of PKC did not alter the pervanadate-induced PLD activation in Rat2 cells. Thus, these results suggest that pervanadate-induced PLD activation is coupled to the transactivation of EGFR by pervanadate resulting in the activation of **p38** MAP ***kinase*** .

CONTROLLED TERM: Medical Descriptors:
*receptor upregulation
enzyme activation
insulin like activity
protein phosphorylation
signal transduction
dose time effect relation
enzyme phosphorylation
protein expression
down regulation
enzyme inhibition
nonhuman
rat
controlled study
animal cell
article
Drug Descriptors:
*epidermal growth factor receptor
*pervanadate
*phospholipase D
protein tyrosine phosphatase inhibitor
cell protein
protein kinase C
genistein
4 (3 chloroanilino) 6,7 dimethoxyquinazoline
protein tyrosine kinase inhibitor
mitogen activated protein kinase
6,7 dimethyl 2 phenylquinoxaline
platelet derived growth factor receptor

stress activated protein kinase
4 (4 fluorophenyl) 2 (4 methylsulfinylphenyl) 5 (4 pyridyl)imidazole
mitogen activated protein kinase inhibitor
2 (2 amino 3 methoxyphenyl)chromone
vanadic acid
hydrogen peroxide

CAS REGISTRY NO.: (phospholipase D) 9001-87-0; (protein kinase C) 141436-78-4; (genistein) 446-72-0; (4 (3 chloroanilino) 6,7 dimethoxyquinazoline) **153436-53-4**; (mitogen activated protein kinase) 142243-02-5; (6,7 dimethyl 2 phenylquinoxaline) 71897-07-9; (stress activated protein kinase) 155215-87-5; (4 (4 fluorophenyl) 2 (4 methylsulfinylphenyl) 5 (4 pyridyl)imidazole) 152121-47-6; (2 (2 amino 3 methoxyphenyl)chromone) 167869-21-8; (vanadic acid) 12260-63-8, 13981-20-9, 37353-31-4; (hydrogen peroxide) 7722-84-1

L41 ANSWER 32 OF 37 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2003037749 EMBASE

TITLE: Stretch enhances contraction of bovine coronary arteries via an NAD(P)H oxidase-mediated activation of the extracellular signal-regulated kinase mitogen-activated protein kinase cascade.

AUTHOR: Oeckler R.A.; Kaminski P.M.; Wolin M.S.

CORPORATE SOURCE: . mike_wolin@nymc.edu

SOURCE: Circulation Research, (10 Jan 2003) 92/1 (23-31).
Refs: 37
ISSN: 0009-7330 CODEN: CIRUAL

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 002 Physiology
018 Cardiovascular Diseases and Cardiovascular Surgery
029 Clinical Biochemistry
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT:

This study examines the effects of an increase in passive stretch in endothelium-removed bovine coronary artery on oxidant-induced changes in force generation. Increasing passive stretch on the arterial segments from 5 to 20 g for 20 minutes caused a subsequent increase (P<0.05) in force generation to 30 mmol/L KCl or 0.1 .mu.mol/L serotonin compared with the prestretch control response. Also associated with the passive stretch were increases in superoxide detection by lucigenin and a selective increase in extracellular signal-regulated kinase (ERK) mitogen-activated protein (MAP) kinase phosphorylation measured by Western analysis. The stretch-induced increase in force generation was eliminated by inhibition of the ERK pathway by the MEK inhibitor PD98059 but not by inhibitors of the **p38** MAP **kinase** pathway (SB202190) or c-Jun N-terminal protein kinase pathway (SP200169). Additionally, stretch-induced increases in both ERK phosphorylation and force generation were attenuated by inhibition of tyrosine kinases (genistein), src (PP2), and specific sites on the epidermal growth factor receptor (EGFR) (AG1478). Probes for oxidant signaling, including NAD(P)H oxidase inhibitors (diphenyliodonium and apocynin) or enhancement of peroxide consumption (ebselen) but not inhibition of xanthine oxidase (allopurinol), attenuated the effects of stretch on both ERK phosphorylation and force generation. Furthermore, stretch caused an increase in EGFR phosphorylation and cytosolic to membrane translocation of the p47phox NAD(P)H oxidase subunit. Hydrogen peroxide also elicited contraction through EGFR phosphorylation and ERK. In summary, stretch seems to enhance force generation via ERK signaling through an

EGFR/src-dependent mechanism activated by peroxide derived from a stretch-mediated activation of the NAD(P)H oxidase, a response that may contribute to hypertensive alterations in vascular reactivity.

CONTROLLED TERM: Medical Descriptors:
*coronary artery
*enzyme activation
*smooth muscle contraction
stretching
cattle
endothelium cell
oxidation
force
mathematical analysis
serotonin release
oxidative stress
enzyme phosphorylation
Western blotting
binding site
signal transduction
cytosol
hypertension
blood vessel reactivity
nonhuman
controlled study
animal tissue
animal cell
article
priority journal
Drug Descriptors:
*reduced nicotinamide adenine dinucleotide phosphate oxidase: EC, endogenous compound
*mitogen activated protein kinase: EC, endogenous compound
mitogen activated protein kinase inhibitor: PD, pharmacology
2 (2 amino 3 methoxyphenyl)chromone: PD, pharmacology
synaptophysin: EC, endogenous compound
4 (4 fluorophenyl) 2 (4 hydroxyphenyl) 5 (4 pyridyl)imidazole: PD, pharmacology
stress activated protein kinase: EC, endogenous compound
enzyme inhibitor: PD, pharmacology
stress activated protein kinase inhibitor: PD, pharmacology
sp 200169: PD, pharmacology
protein tyrosine kinase inhibitor: PD, pharmacology
genistein: PD, pharmacology
protein kinase p60: EC, endogenous compound
epidermal growth factor receptor: EC, endogenous compound
4 (3 chloroanilino) 6,7 dimethoxyquinazoline: PD, pharmacology
diphenyliodonium salt: PD, pharmacology
apocynin: PD, pharmacology
ebselen: PD, pharmacology
xanthine oxidase inhibitor: PD, pharmacology
allopurinol: PD, pharmacology
protein p47: EC, endogenous compound
protein subunit: EC, endogenous compound
hydrogen peroxide: PD, pharmacology
unclassified drug

CAS REGISTRY NO.: (reduced nicotinamide adenine dinucleotide phosphate oxidase) 9032-22-8; (mitogen activated protein kinase) 142243-02-5; (2 (2 amino 3 methoxyphenyl)chromone) 167869-21-8; (4 (4 fluorophenyl) 2 (4 hydroxyphenyl) 5 (4

pyridyl)imidazole) 152121-30-7; (stress activated protein kinase) 155215-87-5; (genistein) 446-72-0; (4 (3 chloroanilino) 6,7 dimethoxyquinazoline) **153436-53-4**; (diphenyliodonium salt) 1483-72-3, 1483-73-4; (apocynin) 498-02-2; (ebselen) 60940-34-3; (allopurinol) 315-30-0; (hydrogen peroxide) 7722-84-1
CHEMICAL NAME: (1) Sb 202190; (2) Pd 98059; (3) Sp 200169; (4) Ag 1478
COMPANY NAME: (3) Sigma; (4) Cell signaling; Fluka

L41 ANSWER 33 OF 37 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2002251244 EMBASE
TITLE: Selective pharmacological inhibitors reveal the role of Syk tyrosine kinase, phospholipase C, phosphatidylinositol-3'-**kinase**, and **p38** mitogen-activated protein **kinase** in Fc receptor-mediated signaling of chicken heterophil degranulation.
AUTHOR: Kogut M.; Lowry V.K.; Farnell M.
CORPORATE SOURCE: M. Kogut, USDA-ARS, Southern Plains Agric. Res. Center, 2881 F and B Road, College Station, TX 77845, United States. kogut@ffsru.tamu.edu
SOURCE: International Immunopharmacology, (2002) 2/7 (963-973). Refs: 52
ISSN: 1567-5769 CODEN: IINMBA
PUBLISHER IDENT.: S 1567-5769(02)00050-4
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
Fc receptors of avian heterophils play a primary role in the elimination of bacterial pathogens in poultry. The cross-linking of Fc receptors with IgG-bacteria complexes results in the secretion of toxic oxygen metabolites and anti-bacterial granules. We have been investigating the upstream signaling events that precede degranulation following crosslinkage of Fc receptors on heterophils. Previously when using the non-selective pharmacological inhibitors genistein, chelerythrine, verapamil, and pertussis toxin, we found no significant inhibitory effects on Fc-mediated heterophil degranulation. In the present studies, we used more selective pharmacological inhibitors to investigate the roles of protein tyrosine kinases, phospholipase C (PLC), phosphatidylinositol 3'-kinase, and the family of mitogen-activated protein kinases (MAPK) on Fc-mediated heterophil degranulation. Inhibitors of the receptor-linked tyrosine kinases (the tryphostins AG 1478 and AG 1296) had no attenuating effects on the Fc receptor-mediated degranulation of chicken heterophils. Likewise, PP2, a selective inhibitor of the Src family of protein tyrosine kinases, had no inhibitory effects on degranulation. However, piceatannol, a selective inhibitor of Syk tyrosine kinase, significantly attenuated the effect of Fc receptor-mediated degranulation. Additionally, Fc-mediated degranulation was significantly attenuated by SB 203580, an inhibitor of p38 MAPK, but not by PD98059, an inhibitor of the extracellular signal-regulated kinase (ERK). An inhibitor of phospholipase C, U73122 and LY294002, an inhibitor of phosphoinositol-3 kinase significantly decreased heterophil degranulation. These results suggest that the Fc receptors on chicken heterophils, like their counterparts on mammalian neutrophils, have no intrinsic tyrosine kinase activity, but probably mediate downstream events through activation of tyrosine-based activation motifs (ITAM). Activation of the Syk tyrosine kinase stimulates downstream phosphorylation of p38 MAPK, phospholipase C, and phosphatidylinositol-3 kinase as signaling pathways that regulate Fc-receptor-mediated degranulation of chicken heterophils. Engaging Fc receptors on chicken heterophils activates a Syk.fwdarw.PLC.fwdarw.PI3-

K.fwdarw.p38 MAPK signal transduction pathway that induces degranulation.

CONTROLLED TERM: Medical Descriptors:
*signal transduction
*degranulation
*neutrophil
chicken
drug effect
enzyme inhibition
enzyme activity
enzyme activation
drug mechanism
enzyme phosphorylation
cell surface
bacterium isolate
nonhuman
controlled study
animal cell
article
priority journal
Drug Descriptors:
*protein tyrosine kinase: EC, endogenous compound
*phospholipase C: EC, endogenous compound
*phosphatidylinositol 3 kinase: EC, endogenous compound
*mitogen activated protein kinase: EC, endogenous compound
*Fc receptor: EC, endogenous compound
*enzyme inhibitor: PD, pharmacology
4 (3 chloroanilino) 6,7 dimethoxyquinazoline: PD, pharmacology
6,7 dimethoxy 3 phenylquinoxaline: PD, pharmacology
quinoxaline derivative: PD, pharmacology
piceatannol: PD, pharmacology
4 (4 fluorophenyl) 2 (4 methylsulfinylphenyl) 5 (4 pyridyl)imidazole: PD, pharmacology
2 (2 amino 3 methoxyphenyl)chromone: PD, pharmacology
1 [[6 (3 methoxyestra 1,3,5(10) trien 17beta yl)amino]hexyl] 1h pyrrole 2,5 dione: PD, pharmacology
2 morpholino 8 phenylchromone: PD, pharmacology
4 amino 5 (4 chlorophenyl) 7 (tert butyl)pyrazolo[3,4]pyrimidine: PD, pharmacology
pyrimidine derivative: PD, pharmacology
protein tyrosine kinase inhibitor: PD, pharmacology
mitogen activated protein kinase inhibitor: PD, pharmacology
phospholipase C inhibitor: PD, pharmacology
phosphatidylinositol 3 kinase inhibitor: PD, pharmacology
unclassified drug
6,7 dimethoxy 2 phenylquinoxaline
pp2

CAS REGISTRY NO.: (protein tyrosine kinase) 80449-02-1; (phospholipase C) 9001-86-9; (phosphatidylinositol 3 kinase) 115926-52-8; (mitogen activated protein kinase) 142243-02-5; (4 (3 chloroanilino) 6,7 dimethoxyquinazoline) **153436-53-4**; (piceatannol) 10083-24-6, 21100-92-5; (4 (4 fluorophenyl) 2 (4 methylsulfinylphenyl) 5 (4 pyridyl)imidazole) 152121-47-6; (2 (2 amino 3 methoxyphenyl)chromone) 167869-21-8; (1 [[6 (3 methoxyestra 1,3,5(10) trien 17beta yl)amino]hexyl] 1h pyrrole 2,5 dione) 112648-68-7; (2 morpholino 8 phenylchromone) 154447-36-6

CHEMICAL NAME: (1) Ag 1478; (2) Ag 1296; (3) Pp2; (4) Sb 203580; (5) Pd

98059; (6) U 73122; (7) Ly 294002
COMPANY NAME: (2) Calbiochem (United States); (7) Sigma

L41 ANSWER 34 OF 37 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2002267242 EMBASE
TITLE: Hyperosmotic stress induces phosphorylation of cytosolic phospholipase A(2) in HaCaT cells by an epidermal growth factor receptor-mediated process.
AUTHOR: Rodriguez I.; Kaszkin M.; Holloschi A.; Kabsch K.; Marques M.M.; Mao X.; Alonso A.
CORPORATE SOURCE: A. Alonso, Deutsches Krebsforschungszentrum, Im Neuenheimer Feld-242, Heidelberg 69120, Germany. A.Alonso@dkfz.de
SOURCE: Cellular Signalling, (2002) 14/10 (839-848).
Refs: 41
ISSN: 0898-6568 CODEN: CESIEY
PUBLISHER IDENT.: S 0898-6568(02)00031-1
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
Cytosolic phospholipase A(2) (cPLA(2)) is an enzyme involved in the formation of proinflammatory mediators by catalyzing the release of arachidonic acid, thereby mediating eicosanoid biosynthesis. Using HaCaT keratinocytes as a model system, we present experimental evidence that in these cells, cPLA(2) is constitutively phosphorylated and that the degree of phosphorylation dramatically increases in cells under hyperosmotic stress induced by sorbitol. In parallel, a rapid release of arachidonic acid followed by prostaglandin E(2) formation was detected. Elucidating the mechanism of cPLA(2) upregulation, we observed that it is mediated via epidermal growth factor receptor (EGFR) activation, since tyrphostin AG1478, a selective inhibitor of EGFR tyrosine kinase, completely inhibited cPLA(2) phosphorylation. Furthermore, addition of PD98059, which is an inhibitor of MEK1 activation, but not of SB203580, which is an inhibitor of **p38** stress **kinase**, inhibited cPLA(2) phosphorylation, indicating that the ras-raf-MEK cascade is the major signalling pathway involved in cPLA(2) phosphorylation. In addition, depletion of the cells from intracellular calcium does not prevent sorbitol-elicited cPLA(2) phosphorylation, suggesting that this process is independent of the presence of calcium. Together, our results demonstrate that hyperosmotic stress phosphorylates cPLA(2) in human keratinocytes by an EGFR-mediated process.

CONTROLLED TERM: Medical Descriptors:
*osmotic stress
cell line
enzyme phosphorylation
cytosol
calcium cell level
drug effect
calcium transport
calcium signaling
human
controlled study
human cell
article
priority journal
Drug Descriptors:
*phospholipase A2
*epidermal growth factor receptor

sorbitol
arachidonic acid: EC, endogenous compound
prostaglandin E2: EC, endogenous compound
4 (3 chloroanilino) 6,7 dimethoxyquinazoline: PD, pharmacology
protein tyrosine kinase inhibitor: PD, pharmacology
epidermal growth factor receptor kinase
2 (2 amino 3 methoxyphenyl)chromone: CM, drug comparison
2 (2 amino 3 methoxyphenyl)chromone: PD, pharmacology
mitogen activated protein kinase inhibitor: PD, pharmacology
4 (4 fluorophenyl) 2 (4 methylsulfinylphenyl) 5 (4 pyridyl)imidazole: CM, drug comparison
4 (4 fluorophenyl) 2 (4 methylsulfinylphenyl) 5 (4 pyridyl)imidazole: PD, pharmacology
calcium ion

CAS REGISTRY NO.: (phospholipase A2) 9001-84-7; (sorbitol) 26566-34-7, 50-70-4, 53469-19-5; (arachidonic acid) 506-32-1, 6610-25-9, 7771-44-0; (prostaglandin E2) 363-24-6; (4 (3 chloroanilino) 6,7 dimethoxyquinazoline) **153436-53-4**; (epidermal growth factor receptor kinase) 79079-06-4; (2 (2 amino 3 methoxyphenyl)chromone) 167869-21-8; (4 (4 fluorophenyl) 2 (4 methylsulfinylphenyl) 5 (4 pyridyl)imidazole) 152121-47-6; (calcium ion) 14127-61-8

CHEMICAL NAME: (1) Pd 98059; (2) Ag 1478; (3) Sb 203580

COMPANY NAME: (3) Calbiochem (Germany)

L41 ANSWER 35 OF 37 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2003091304 EMBASE

TITLE: Protein kinase inhibitors from the urea class.

AUTHOR: Dumas J.

CORPORATE SOURCE: J. Dumas, Bayer Research Center, Bayer Corporation, Pharmaceutical Division, 400 Morgan Lane, West Haven, CT 06516, United States. jacques.dumas.b@bayer.com

SOURCE: Current Opinion in Drug Discovery and Development, (2002) 5/5 (718-727).
Refs: 74
ISSN: 1367-6733 CODEN: CODDFF

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT:
016 Cancer
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT:

Protein kinase inhibitors hold great potential as novel therapies for cancer and inflammatory disorders. While bis-aryl ureas have been reported as kinase inhibitors as early as 1996, a number of publications and patent applications appeared in the literature during the past two years. Three urea-based kinase inhibitors are currently undergoing clinical trials. The present review summarizes available data, and provides an overview of the structure-activity relationships against a variety of **kinase** targets, including ***p38*** , Raf-1 and cyclin-dependent kinases.

CONTROLLED TERM: Medical Descriptors:
*enzyme inhibition
*angiogenesis

*cell cycle
drug research
drug structure
structure activity relation
drug targeting
drug protein binding
antineoplastic activity
antiinflammatory activity
cancer chemotherapy
liver cell carcinoma: DT, drug therapy
kidney carcinoma: DT, drug therapy
arthritis: DT, drug therapy
inflammation
drug efficacy
drug safety
diarrhea: SI, side effect
rash: SI, side effect
fatigue: SI, side effect
human
nonhuman
mouse
clinical trial
phase 1 clinical trial
phase 2 clinical trial
animal model
human cell
review
Drug Descriptors:
*protein kinase inhibitor: AE, adverse drug reaction
*protein kinase inhibitor: CT, clinical trial
*protein kinase inhibitor: AD, drug administration
*protein kinase inhibitor: AN, drug analysis
*protein kinase inhibitor: CR, drug concentration
*protein kinase inhibitor: DV, drug development
*protein kinase inhibitor: DO, drug dose
*protein kinase inhibitor: DT, drug therapy
*protein kinase inhibitor: PK, pharmacokinetics
*protein kinase inhibitor: PD, pharmacology
*protein kinase inhibitor: IV, intravenous drug administration
*protein kinase inhibitor: PO, oral drug administration
*urea derivative: AE, adverse drug reaction
*urea derivative: CT, clinical trial
*urea derivative: AD, drug administration
*urea derivative: AN, drug analysis
*urea derivative: CR, drug concentration
*urea derivative: DV, drug development
*urea derivative: DO, drug dose
*urea derivative: DT, drug therapy
*urea derivative: PK, pharmacokinetics
*urea derivative: PD, pharmacology
*urea derivative: IV, intravenous drug administration
*urea derivative: PO, oral drug administration
*cyclin dependent kinase inhibitor: CT, clinical trial
*cyclin dependent kinase inhibitor: AN, drug analysis
*cyclin dependent kinase inhibitor: DV, drug development
*cyclin dependent kinase inhibitor: PD, pharmacology
*bay 43 9006: AE, adverse drug reaction
*bay 43 9006: CT, clinical trial
*bay 43 9006: AD, drug administration
*bay 43 9006: AN, drug analysis
*bay 43 9006: DV, drug development

*bay 43 9006: DO, drug dose
*bay 43 9006: DT, drug therapy
*bay 43 9006: PD, pharmacology
*bay 43 9006: PO, oral drug administration
*birb 796: CT, clinical trial
*birb 796: AN, drug analysis
*birb 796: DV, drug development
*birb 796: DO, drug dose
*birb 796: DT, drug therapy
*birb 796: PD, pharmacology
*birb 796: IV, intravenous drug administration
*cp 547632: CT, clinical trial
*cp 547632: AD, drug administration
*cp 547632: AN, drug analysis
*cp 547632: CR, drug concentration
*cp 547632: DV, drug development
*cp 547632: DO, drug dose
*cp 547632: DT, drug therapy
*cp 547632: PK, pharmacokinetics
*cp 547632: PD, pharmacology
*cp 547632: PO, oral drug administration
enzyme inhibitor: AE, adverse drug reaction
enzyme inhibitor: CT, clinical trial
enzyme inhibitor: AN, drug analysis
enzyme inhibitor: CR, drug concentration
enzyme inhibitor: DV, drug development
enzyme inhibitor: DO, drug dose
enzyme inhibitor: DT, drug therapy
enzyme inhibitor: PK, pharmacokinetics
enzyme inhibitor: PD, pharmacology
protein tyrosine kinase inhibitor: CT, clinical trial
protein tyrosine kinase inhibitor: AN, drug analysis
protein tyrosine kinase inhibitor: DV, drug development
protein tyrosine kinase inhibitor: PD, pharmacology
imatinib: CT, clinical trial
gefitinib: CT, clinical trial
erlotinib: CT, clinical trial
flavopiridol: CT, clinical trial
mitogen activated protein kinase inhibitor: CT, clinical trial
mitogen activated protein kinase inhibitor: AN, drug analysis
mitogen activated protein kinase inhibitor: DV, drug development
mitogen activated protein kinase inhibitor: PD, pharmacology
vx 745: DV, drug development
rw 67657: DV, drug development
ruboxistaurin: DV, drug development
epidermal growth factor receptor kinase
quinazoline derivative: DV, drug development
antiinflammatory agent: CT, clinical trial
antiinflammatory agent: AD, drug administration
antiinflammatory agent: AN, drug analysis
antiinflammatory agent: DV, drug development
antiinflammatory agent: DO, drug dose
antiinflammatory agent: DT, drug therapy
antiinflammatory agent: PD, pharmacology
antiinflammatory agent: IV, intravenous drug administration

unclassified drug
4 [4 (4 fluorophenyl) 1 (3 phenylpropyl) 5 (4 pyridinyl) 1h imidazol 2 yl] 3 butyn 1 ol

CAS REGISTRY NO.: (imatinib) 152459-95-5, 220127-57-1; (gefitinib) **184475-35-2**, **184475-55-6**, **184475-56-7**; (erlotinib) **183319-69-9**; (flavopiridol) 146426-40-6; (ruboxistaurin) 169939-93-9, 169939-94-0; (epidermal growth factor receptor kinase) 79079-06-4

CHEMICAL NAME: (1) Bay 43 9006; (2) Vx 745; (3) Birb 796; (4) Cp 547632; (5) Zd 1839; (6) Osi 774; (7) Rwj 67657; (8) Ly 333531; Glivec

COMPANY NAME: (1) Bayer; (2) Vertex; (3) Boehringer Ingelheim; (4) Pfizer; (5) Astra Zeneca; (6) Osi; (7) RW Johnson; (8) Lilly; Aventis; Glaxo SmithKline; BASF; Amgen; Banyu; Pharmacia Upjohn; Sugen

L41 ANSWER 36 OF 37 EMBASE
on STN

ACCESSION NUMBER: 2001430965 EMBASE

TITLE: Human cervical cancer cells use Ca(2+) signalling, protein tyrosine phosphorylation and MAP kinase in regulatory volume decrease.

AUTHOR: Shen M.-R.; Chou C.-Y.; Browning J.A.; Wilkins R.J.; Ellory J.C.

CORPORATE SOURCE: J.C. Ellory, University Laboratory of Physiology, Parks Road, Oxford OX1 3PT, United Kingdom.
clive.ellory@physiol.ac.uk

SOURCE: Journal of Physiology, (1 Dec 2001) 537/2 (347-362).
Refs: 42
ISSN: 0022-3751 CODEN: JPHYA7

COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT:
1. This study was aimed at identifying the signalling pathways involved in the activation of volume-regulatory mechanisms of human cervical cancer cells. 2. Osmotic swelling of human cervical cancer cells induced a substantial increase in intracellular Ca(2+) ([Ca(2+)](i)) by the activation of Ca(2+) entry across the cell membrane, as well as Ca(2+) release from intracellular stores. This Ca(2+) signalling was critical for the normal regulatory volume decrease (RVD) response. 3. The activation of swelling-activated ion and taurine transport was significantly inhibited by tyrosine kinase inhibitors (genistein and tyrphostin AG 1478) and potentiated by the tyrosine phosphatase inhibitor Na(3)VO(4). However, the Src family of tyrosine kinases was not involved in regulation of the swelling-activated Cl(-) channel. 4. Cell swelling triggered mitogen-activated protein (MAP) kinase cascades leading to the activation of extracellular signal-regulated kinase 1 and 2 (ERK1/ERK2) and **p38** ***kinase*** . The volume-responsive ERK1/ERK2 signalling pathway linked with the activation of K(+) and Cl(-) channels, and taurine transport. However, the volume-regulatory mechanism was independent of the activation of **p38** MAP **kinase**. 5. The phosphorylated ERK1/ERK2 expression following a hypotonic shock was up-regulated by protein kinase C (PKC) activator phorbol 12-myristate 13-acetate (PMA) and down-regulated by PKC inhibitor staurosporine. The response of ERK activation to hypotonicity also required Ca(2+) entry and depended on tyrosine kinase and mitogen-activated/ERK-activating kinase (MEK) activity. 6. Considering the results overall, osmotic swelling promotes the activation of tyrosine kinase and ERK1/ERK2 and raises intracellular Ca(2+), all of which play a crucial role in the volume-regulatory

mechanism of human cervical cancer cells.

CONTROLLED TERM: Medical Descriptors:
*calcium signaling
*uterine cervix cancer
protein phosphorylation
cancer cell culture
osmosis
calcium cell level
calcium transport
cell membrane
chloride channel
cell swelling
extracellular space
signal transduction
potassium channel
protein expression
shock
enzyme regulation
muscle hypotonia
human
controlled study
human cell
article
priority journal
Drug Descriptors:
*tyrosine: EC, endogenous compound
*mitogen activated protein kinase: EC, endogenous compound
*calcium ion: EC, endogenous compound
taurine: EC, endogenous compound
protein tyrosine kinase inhibitor
genistein
4 (3 chloroanilino) 6,7 dimethoxyquinazoline
protein tyrosine kinase: EC, endogenous compound
mitogen activated protein kinase kinase: EC, endogenous compound
synaptophysin: EC, endogenous compound
protein kinase: EC, endogenous compound
protein kinase C activator
phorbol 13 acetate 12 myristate

CAS REGISTRY NO.: (tyrosine) 16870-43-2, 55520-40-6, 60-18-4; (mitogen activated protein kinase) 142243-02-5; (calcium ion) 14127-61-8; (taurine) 107-35-7; (genistein) 446-72-0; (4 (3 chloroanilino) 6,7 dimethoxyquinazoline) **153436-53-4**; (protein tyrosine kinase) 80449-02-1; (mitogen activated protein kinase kinase) 142805-58-1; (protein kinase) 9026-43-1; (phorbol 13 acetate 12 myristate) 16561-29-8

L41 ANSWER 37 OF 37 EMBASE
on STN

ACCESSION NUMBER: 2001078448 EMBASE
TITLE: Regulation of p42/p44 MAPK and p38 MAPK by the adenosine A(1) receptor in DDT(1)MF-2 cells.
AUTHOR: Robinson A.J.; Dickenson J.M.
CORPORATE SOURCE: J.M. Dickenson, Department of Life Sciences, Faculty of Science and Mathematics, Nottingham Trent University, Clifton Lane, Nottingham NG11 8NS, United Kingdom. john.dickenson@ntu.ac.uk
SOURCE: European Journal of Pharmacology, (16 Feb 2001) 413/2-3 (151-161).
Refs: 44

ISSN: 0014-2999 CODEN: EJPHAZ
PUBLISHER IDENT.: S 0014-2999(01)00761-0
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT:
The mitogen-activated protein kinase (MAPK) family consists of the p42/p44 MAPKs and the stress-activated protein kinases, c-Jun N-terminal **kinase** (JNK) and **p38** MAPK. We have previously reported that the human adenosine A(1) receptor stimulates p42/p44 MAPK in transfected Chinese hamster ovary cells. In this study, we have investigated whether the endogenous adenosine A(1) receptor in the smooth muscle cell line, DDT(1)MF-2 activates p42/p44 MAPK, JNK and p38 MAPK. The adenosine A(1) receptor agonist N(6)-cyclopentyladenosine stimulated time and concentration-dependent increases in p42/p44 MAPK and p38 MAPK phosphorylation in DDT(1)MF-2 cells. No increases in JNK phosphorylation were observed following adenosine A(1) receptor activation. N(6)-cyclopentyladenosine-mediated increases in p42/p44 MAPK and p38 MAPK phosphorylation were blocked by the selective adenosine A(1) receptor antagonist 1,3-dipropylcyclopentylxanthine and following pretreatment of cells with pertussis toxin. Furthermore, adenosine A(1) receptor-mediated increases in p42/p44 MAPK were sensitive to the MAPK kinase 1 inhibitor PD 98059 (2'-amino-3'-methoxyflavone), whereas p38 MAPK responses were blocked by the p38 MAPK inhibitor SB 203580 (4-(4-fluorophenyl)-2-(4-methylsulfinylphenyl)-5-(4-pyridyl)1H-imidazole). The broad range protein tyrosine kinase inhibitors genistein and tyrphostin A47 (.alpha.-cyano-(3,4-dihydroxy)thiocinnamide) did not block adenosine A(1) receptor stimulation of p42/p44 MAPK. For comparison, insulin-mediated increases in p42/p44 MAPK were blocked by genistein and tyrphostin A47. The Src tyrosine kinase inhibitor PP2 (4-amino-5-(4-chlorophenyl)-7-(t-butyl)pyrazolo[3,4-d]pyrimidine) and the epidermal growth factor receptor tyrosine kinase inhibitor AG1478 (4-(3-chloroanilino)-6,7-dimethoxyquinazoline) also had no effect on adenosine A(1) receptor stimulation of p42/p44 MAPK. Furthermore, the protein kinase C inhibitors Ro 31-8220 (3-{1-[3-(2-isothioureido) propyl]indol-3-yl}-4-(1-methylindol-3-yl)-3-pyrrolin-2,5-dione), chelerythrine and GF 109203X (2-[1-(3-dimethylaminopropyl)-1H-indol-3-yl]-3-(1H-indol-3-yl)-maleimide) were without effect on adenosine A(1) receptor-induced p42/p44 MAPK phosphorylation. In contrast, wortmannin and LY 294002 (2-(4-morpholinyl)-8-phenyl-4H-1-benzopyran-4-one), inhibitors of phosphatidylinositol 3-kinase, attenuated adenosine A(1) receptor stimulation of p42/p44 MAPK phosphorylation. In conclusion, the adenosine A(1) receptor stimulates p42/p44 MAPK through a pathway which appears to be independent of tyrosine kinase activation but involves phosphatidylinositol 3-kinase. Finally, adenosine A(1) receptor stimulation in DDT(1)MF-2 cells also activated p38 MAPK but not JNK via a pertussis toxin-sensitive pathway. .COPYRGT. 2001 Elsevier Science B.V.

CONTROLLED TERM: Medical Descriptors:
hamster
ovary cell
smooth muscle fiber
cell line
concentration response
phosphorylation
enzyme activation
drug receptor binding
nonhuman
controlled study
animal cell
article
priority journal

Drug Descriptors:
*protein p44: EC, endogenous compound
*protein p42: EC, endogenous compound
*stress activated protein kinase: EC, endogenous compound
*synaptophysin: EC, endogenous compound
*mitogen activated protein kinase: EC, endogenous compound
*adenosine A1 receptor: EC, endogenous compound
adenosine A1 receptor agonist: PD, pharmacology
n cyclopentyladenosine: PD, pharmacology
adenosine A1 receptor antagonist: PD, pharmacology
1,3 dipropylcyclopentylxanthine: PD, pharmacology
pertussis toxin
2 (2 amino 3 methoxyphenyl)chromone: PD, pharmacology
4 (4 fluorophenyl) 2 (4 methylsulfinylphenyl) 5 (4 pyridyl)imidazole: PD, pharmacology
genistein: PD, pharmacology
tyrphostin: PD, pharmacology
insulin
protein tyrosine kinase inhibitor: PD, pharmacology
4 (3 chloroanilino) 6,7 dimethoxyquinazoline: PD, pharmacology
2 [1 (3 amidinothiopropyl) 1h indol 3 yl] 3 (1 methyl 1h indol 3 yl)maleimide: PD, pharmacology
chelerythrine: PD, pharmacology
2 [1 (3 dimethylaminopropyl) 3 indolyl] 3 (3 indolyl)maleimide: PD, pharmacology
wortmannin: PD, pharmacology
2 morpholino 8 phenylchromone: PD, pharmacology
mitogen activated protein kinase inhibitor: PD, pharmacology
protein kinase C inhibitor: PD, pharmacology
unclassified drug

CAS REGISTRY NO.: (stress activated protein kinase) 155215-87-5; (mitogen activated protein kinase) 142243-02-5; (pertussis toxin) 70323-44-3; (2 (2 amino 3 methoxyphenyl)chromone) 167869-21-8; (4 (4 fluorophenyl) 2 (4 methylsulfinylphenyl) 5 (4 pyridyl)imidazole) 152121-47-6; (genistein) 446-72-0; (insulin) 9004-10-8; (4 (3 chloroanilino) 6,7 dimethoxyquinazoline) **153436-53-4**; (2 [1 (3 amidinothiopropyl) 1h indol 3 yl] 3 (1 methyl 1h indol 3 yl)maleimide) 125314-64-9; (chelerythrine) 34316-15-9; (2 [1 (3 dimethylaminopropyl) 3 indolyl] 3 (3 indolyl)maleimide) 133052-90-1; (wortmannin) 19545-26-7; (2 morpholino 8 phenylchromone) 154447-36-6

CHEMICAL NAME: (1) Ag 1478; (2) Gf 109203x; (3) Ly 294002; (4) Pd 98059; (5) Ro 31 8220; (6) Sb 203580

COMPANY NAME: (6) Calbiochem (United Kingdom)

=> fil reg
FILE 'REGISTRY' ENTERED AT 12:55:50 ON 04 JUN 2004
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STRUCTURE FILE UPDATES: 3 JUN 2004 HIGHEST RN 689216-09-9
DICTIONARY FILE UPDATES: 3 JUN 2004 HIGHEST RN 689216-09-9

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

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http://www.cas.org/ONLINE/DBSS/registryss.html

=> s 153436-53-4 or 184475-35-2 or 184475-55-6 or 184475-56-7 or 183319-69-9 or
183321-74-6 or 170449-18-0

1 153436-53-4
(153436-53-4/RN)
1 184475-35-2
(184475-35-2/RN)
1 184475-55-6
(184475-55-6/RN)
1 184475-56-7
(184475-56-7/RN)
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(183319-69-9/RN)
1 183321-74-6
(183321-74-6/RN)
1 170449-18-0
(170449-18-0/RN)
L42 7 153436-53-4 OR 184475-35-2 OR 184475-55-6 OR 184475-56-7 OR
183319-69-9 OR 183321-74-6 OR 170449-18-0

Structures for hit RNs from Medline & Embase

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L42 ANSWER 1 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN
RN **184475-56-7** REGISTRY
CN 4-Quinazolinamine, N-(3-chloro-4-fluorophenyl)-7-methoxy-6-[3-(4-
morpholinyl)propoxy]-, dihydrochloride (9CI) (CA INDEX NAME)
MF C22 H24 Cl F N4 O3 . 2 Cl H
SR CA
LC STN Files: BIOTECHNO, CA, CAPLUS, EMBASE, IMSPATENTS, IMSRESEARCH,
PROUSDDR, SYNTHLINE, TOXCENTER, USPATFULL
DT.CA CAplus document type: Patent
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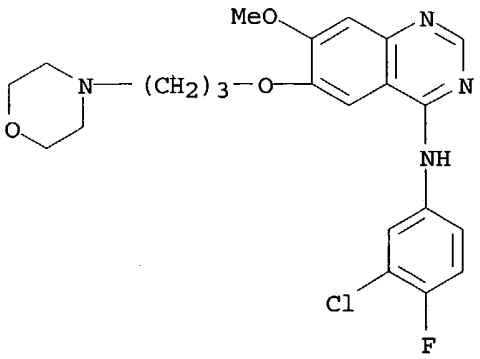
CRN (184475-35-2)



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1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L42 ANSWER 2 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN
RN **184475-55-6** REGISTRY
CN 4-Quinazolinamine, N-(3-chloro-4-fluorophenyl)-7-methoxy-6-[3-(4-morpholinyl)propoxy]-, monohydrochloride (9CI) (CA INDEX NAME)
MF C22 H24 Cl F N4 O3 . Cl H
SR CA
LC STN Files: BIOTECHNO, CA, CAPLUS, EMBASE, IMSPATENTS, IMSRESEARCH, PROUSDDR, SYNTHLINE, TOXCENTER, USPATFULL
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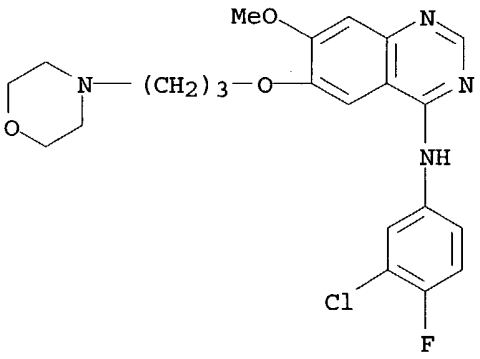
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
CRN (184475-35-2)



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1 REFERENCES IN FILE CA (1907 TO DATE)
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L42 ANSWER 3 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN

RN **184475-35-2** REGISTRY
CN 4-Quinazolinamine, N-(3-chloro-4-fluorophenyl)-7-methoxy-6-[3-(4-morpholinyl)propoxy]- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 4-(3'-Chloro-4'-fluoroanilino)-7-methoxy-6-(3-morpholinopropoxy)quinazoline
CN Gefitinib
CN Iressa
CN ZD 1839
FS 3D CONCORD
MF C22 H24 Cl F N4 O3
CI COM
SR CA
LC STN Files: ADISINSIGHT, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CHEMCATS, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, PHAR, PROUSDDR, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
DT.CA CAplus document type: Book; Conference; Journal; Patent
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RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
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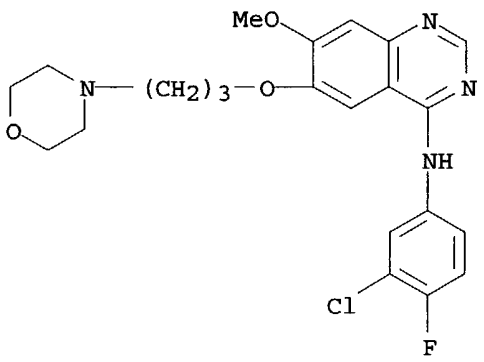

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255 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
256 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L42 ANSWER 4 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN
RN **183321-74-6** REGISTRY
CN 4-Quinazolinamine, N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Erlotinib
CN NSC 718781
CN OSI 744

CN R 1415
FS 3D CONCORD
MF C22 H23 N3 O4
CI COM
SR CA
LC STN Files: ANABSTR, BIOSIS, CA, CAPLUS, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, MRCK*, PROUSDDR, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
DT.CA CAplus document type: Book; Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); FORM (Formation, nonpreparative); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
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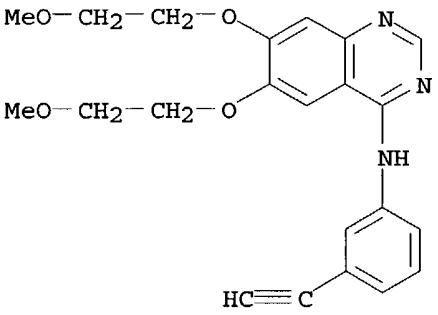

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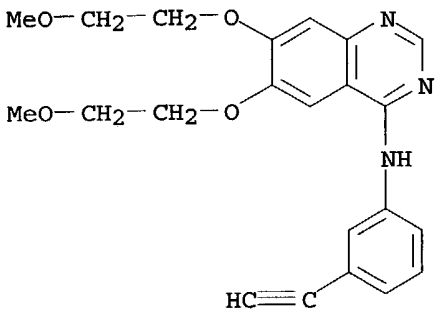
32 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
33 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L42 ANSWER 5 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN
RN **183319-69-9** REGISTRY
CN 4-Quinazolinamine, N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-, monohydrochloride (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 6,7-Bis(2-methoxyethoxy)-4-(3-ethynylanilino)quinazoline hydrochloride
CN CP 358774
CN OSI 774
CN Tarceva
MF C22 H23 N3 O4 . Cl H
SR CA
LC STN Files: ADISINSIGHT, ANABSTR, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, EMBASE, IMSPATENTS, IMSRESEARCH, IPA, MRCK*, PHAR, PROUSDDR, SYNTHLINE, TOXCENTER, USAN, USPATFULL
(*File contains numerically searchable property data)
DT.CA CAplus document type: Conference; Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT

(Reactant or reagent); USES (Uses)
CRN (183321-74-6)



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82 REFERENCES IN FILE CA (1907 TO DATE)
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L42 ANSWER 6 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN
RN **170449-18-0** REGISTRY
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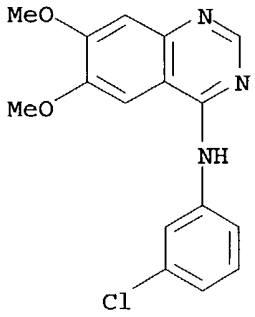
MF C16 H14 Cl N3 O2 . Cl H
SR CA
LC STN Files: ANABSTR, CA, CANCERLIT, CAPLUS, MEDLINE, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
CRN (153436-53-4)



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7 REFERENCES IN FILE CA (1907 TO DATE)

7 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L42 ANSWER 7 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN
RN **153436-53-4** REGISTRY
CN 4-Quinazolinamine, N-(3-chlorophenyl)-6,7-dimethoxy- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN AG 1478
CN NSC 693255
CN Tyrphostin AG 1478
FS 3D CONCORD
DR 175178-82-2
MF C16 H14 Cl N3 O2
CI COM
SR CA
LC STN Files: BIOSIS, BIOTECHNO, CA, CAPLUS, CHEMCATS, CIN, CSCHEM, EMBASE, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); USES (Uses)
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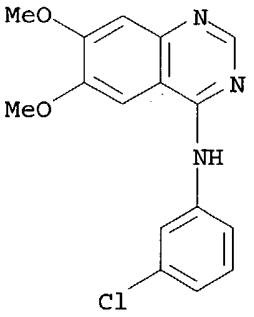

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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80 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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